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A
CLINICAL HANDBOOK
OF
URINE ANALYSIS.

WORKS BY THE SAME AUTHOR.

A SYNOPSIS OF PRACTICAL CHEMISTRY (QUALITATIVE), INORGANIC AND ORGANIC. 2nd Edition, 1902, pp. 193. Price 4s. 6d. net.

This work-book is arranged with the view of presenting, as briefly and in as simple a form as possible, the tests for Inorganic and Organic substances conducted in the usual Courses of Practical Chemistry. The instructions are, as far as possible, in tabular form, or the analysis is described step by step in the simplest possible manner. It is specially suited to the requirements of medical and science students. The book has been pronounced by many leading chemical teachers to be the best arranged and simplest book on the subject in English. It has been adopted in various Universities and Medical Schools, and has been translated into several languages.

THE SYMPTOMS AND TREATMENT OF POISONING. Published (1903) by Government and Adopted in Government Hospitals in India. Price 1s. 8d. net.

It contains the symptoms and treatment of the various Poisons briefly and clearly arranged in alphabetical order.

A
CLINICAL HANDBOOK
OF
URINE ANALYSIS.

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PREFACE.

An attempt has been made in the following pages to place before the clinical student and medical practitioner the essentials of clinical urine analysis in a *brief, simple, and convenient form.*

The methods described are, as a rule, those which have been most fully studied, and which are at present considered the most suitable for *clinical* requirements.

The first edition of this book was published only in India, and has been supplied by the various Local Governments to all Civil Hospitals in India, as well as by the Military Authorities to all British Army Hospitals in that country. In addition, the rapid exhaustion of a specially large edition appears to indicate that the book has been found of service by medical men.

The present edition has been amplified by about sixty pages, and further, an entirely new set of illustrations has been prepared for it.

I have to thank Dr. Noël Paton, Superintendent of the Research Laboratories of the Royal College of Physicians, Edinburgh; Dr. Malcolm, Lecturer on Physiological Chemistry, Edinburgh University; and Dr. Alexander

Bruce, Physician to the Edinburgh Royal Infirmary, for advice on certain points; also Professor Halliburton, London, and Messrs. Longmans, Green & Co., London, for permission to reproduce the diagram of Maltosazone and Lactosazone crystals from "The Essentials of Chemical Physiology;" also Professor T. H. Milroy and Dr. J. A. Milroy, of Queen's College, Belfast, for permission to reproduce the plates illustrating various spectra from their "Practical Physiological Chemistry," and for the loan of the necessary blocks; and Mr. A. Frazer, Edinburgh, for the loan of the blocks representing Doremus Ureometers.

My thanks are also due to Messrs. Wallace, C.M.G., and Cathcart, Surgeons to the Edinburgh Royal Infirmary; and to Dr. F. D. Boyd, C.M.G., Assistant-Physician to that Institution, for several references to the literature of Cryoscopy.

I much regret that I have been obliged to omit references, as a rule: this has been necessitated by my having to use the available space for footnotes explaining or qualifying points in the text. A bibliography has also been omitted in view of the vast dimensions of the literature of the subject. Such information is, further, somewhat beyond the scope of this small book.

C. H. BEDFORD.

EDINBURGH, *February*, 1904.

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ABBREVIATIONS.

ppt.	precipitate.
pptd.	precipitated.
c.c.	cubic centimetre.
sp. gr.	specific gravity.
Am.*	Ammonium.
Am.-Mg.	Ammonio-Magnesium.
NaOH	Caustic Soda.
KOH	Caustic Potash.
HNO_3	Nitric Acid.
H_2SO_4	Sulphuric Acid.
$^{\circ}/_{\circ}$	per centum.
=	"it indicates" or "there results."
Liq.	Liquor.
sol.	soluble.
insol.	insoluble.
grm.	gramme.
gr.	grain.

The symbols of the elements (*e.g.*, Ca, K, Na) have been freely employed for the sake of economising space and for clearness.

* *Am* is used merely as an abbreviation—*i.e.*, the chemical significance attending the employment of NH_4 is not to be attached to it.

COLLECTION FOR ANALYSIS.

For an ordinary Qualitative Examination.—*Whenever possible, a sample from the collected secretion of the twenty-four hours should be examined.* The patient is directed to empty the bladder at, say, 8 A.M., and to reject that specimen. All urine voided thereafter up to (and inclusive of) that passed at 8 A.M. on the following morning is to be kept, *the patient being directed before defæcation to empty the bladder into a separate vessel.*

[*To minimise putrefactive changes in the collected urine*—(*a*) use a *perfectly clean glass bottle* (glass-stoppered Winchester quarts which hold half-a-gallon are to be preferred for a twenty-four hours' specimen).

(*b*) Place a small quantity of Toluol in the bottle to prevent putrefactive changes. Or the bottle may be packed round with ice, or placed in a refrigerator, so as to keep the temperature below 4° C.

(*c*) Where possible, the urine should be passed directly into the bottle, in the mouth of which a large glass funnel should be placed.

(*d*.) The bottle should be re-stoppered after each addition of urine.

(*e*.) It should be placed in a cool dark room.

Other "preservatives," such as chloroform or chloral, should not be used, as these substances are reducing agents, and would interfere with the examination—*e.g.*, for sugar by Fehling's solution. Salicylic acid and Resorcin interfere with the albumin tests.]

The collected secretion is then measured, the sample agitated in order to mix it thoroughly, and about a pint of it sent for examination.

By examining a sample from the twenty-four hours' collection many errors will be avoided, such as overlooking albumin, sugar, tube-casts, &c., as these may only be found (or may be more plentiful) at certain times of day in the urine.

IF IT IS IMPRACTICABLE TO OBTAIN A TWENTY-FOUR HOURS' SAMPLE, then—(*a*) take a sample passed *about three hours after breakfast;* and (*b*) another passed on rising in the morning. Examine these separately, so as to obtain information as to the effects of rest, fasting, and of taking food.

IF ONLY ONE SAMPLE CAN BE OBTAINED, take that passed three hours after breakfast.

Never rely alone on the examination of the urine passed on rising in the morning, for albumin and sugar may be absent then and be abundant three or four hours after breakfast.

Never attach too much importance to the result of a single examination of the urine, even if negative in character.

It may be as well to warn the patient against spitting into the urine to be examined, as in testing for blood or albumin this may cause misleading results.

IN SENDING SAMPLES OF URINE FROM A DISTANCE for examination, send the bottle *packed in ice;* or add two drops of toluol or formalin for each ounce of urine sent.* This will preserve the urine for several days, even in tropical heat. It is, further, a good plan to *fill the bottle* containing the sample *quite full*, as this lessens the amount of disturbance by shaking, and diminishes the consequent risk of breaking-up such objects as brittle tube-casts, &c.

For a Quantitative Examination it is specially necessary that a sample from the collected twenty-four hours' secretion be examined.

If the urine is to be specially examined for Pus *or* "Gonorrhœal threads," examine the specimen passed on rising in the morning. Pus and "threads" collect during sleep, and are washed out with the first discharge of urine.

It is often advisable to direct the patient to pass about a couple of ounces of urine into a separate vessel; and then to pass the rest separately. By examining these two portions separately, information may be obtained as to the urethral origin of the pus, &c.

As regards Pus, Renal Epithelium, Spermatozoa, or Tube-casts the search should, in general, be made for these as soon as possible after the urine has been passed, as under certain conditions these objects may become disintegrated or altered. This is specially the case in *alkaline* urines. So it is best to centrifugalise such alkaline urines when voided and straightway examine the sediment. On the other hand, urines with an *acid* reaction should be allowed to settle naturally (for three or four hours), as this removes any risk of damage from centrifugalising, and the above-named objects retain their appearances well for some time in acid urines.

---

* Formalin is a 40 per cent. solution of Formaldehyde in water. It is a powerful reducing agent, and precipitates albumin when added in relatively large proportions. The author has satisfied himself by repeated experiments that the proportion above recommended is too small to interfere in any way with the analysis of the urine.

When searching for tubercle bacilli, centrifugalise the urine as soon as possible after being voided.

IF SPECIALLY TO BE EXAMINED FOR ALBUMIN direct the patient to reject the first two ounces passed, and then to void the rest into a separate vessel for examination.

IN LIFE ASSURANCE CASES, examination for certain employments or for any particular purpose where it is necessary to guard against substitution of another sample by the examinee :

(*a.*) Direct the patient to call at a time so fixed as to be about three hours after a meal.

(*b.*) If practicable, the sample should then be passed in the physician's presence.

(*c.*) Where this is impracticable, and the urine is passed in an adjoining room, take the urine's temperature at once. This, a minute or so after being voided, is generally about two or three degrees Fahrenheit below the normal body temperature.

(*d.*) If the examination of the sample is inconclusive, obtain a sample from the twenty-four hours' collected urine, and then compare its indications with those of the sample first examined.

SCHEME OF URINE ANALYSIS.

SCHEME OF

Ordinary Routine Examination.	Routine Methods.
A. Physical Characters. (Note quantity passed during the 24 hours.)	
1. Colour.	By Vogel's Scale.
2. Odour.	
3. Appearance (transparency, consistence, opalescence, suspended matter)	By the application of heat and various reagents to distinguish the presence in excess of Urates, Phosphates, Oxalates, Carbonates, Mucus, or of Pus or Bacteria.
4. Deposit.	
5. Specific Gravity .	Urinometer.

URINE ANALYSIS.

Quantitative Methods.

Urea. Hüfner's process using—

- (*a*) Doremus's tube.
- (*b*) Dupré's method.

Total Purin Bodies. By Hall's purinometer.

Uric acid.

- (*a*) Piperidine process, or
- (*b*) Hopkins's method.

Phosphates. Uranium process.

Oxalates. Autenreith's method.

Chlorides. Sutton-Mohr's process.

SCHEME OF

Ordinary Routine Examination.	Routine Methods.
B. Chemical Characters.	
1. Reaction . .	By litmus papers.
2. Albumin . .	(*a*) Heat. (*b*) Nitric acid. (*c*) Picric acid.
3. Sugar . . .	(*a*) Safranine or Fehling. (*b*) Phenyl-hydrazine.
4. Bile . . .	*Acids.* Oliver's test. *Pigments.* Gmelin's or Huppert's.
5. Hœmoglobin . .	Guaiac or Heller's.
C. Microscopical Characters.	

URINE ANALYSIS.

Special Examination.	Quantitative Methods.
(Tanret's test for further confirmatory purposes).	
Salicyl-Sulphonic Acid (for rapid differentiation of albumins and albumoses).	Esbach's tube.
Globulins.	
Proteoses (albumoses).	
Peptones.	
Fibrin.	
(If presence of other reducing substances is suspected, perform Fermentation test.)	(*a*) Pavy's or Fehling's Process.
Acetone.	(*b*) Polarimetry.
Aceto-acetic acid.	
Glycuronic acid.	
Chyle.	Cryoscopy.
Fibrin.	
Indican.	
Diazo Reaction.	Urobilin.
Drug-tests of Renal Excretory power.	
Tubercle bacillus.	
Gonococcus.	

PART I.

QUALITATIVE EXAMINATION.

QUANTITY.

A healthy adult *male* excretes 1000–1500 cubic centimetres per diem—usually about 50 ozs. (1450 c.c.).

A healthy adult *female* excretes 900–1200 c.c.

" " child excretes *approximately* twice as many ounces as its years between 2 and 12 years of age—*i.e.*, at 2 it excretes 4 ozs., at 8, 16 ozs., &c.

Normally, more urine is secreted during the day time, —about six times as much as at night.*

For adults the *daily minimum* may normally fall to about 500 c.c. (15 ozs.). The *daily maximum* may normally rise as high as about 2500 c.c. (75 ozs.).

[*Diminution* of the amount is caused by :—

(*a*) Profuse sweating; (*b*) Diarrhœa or violent hæmorrhage; (*c*) a relative excess of non-nitrogenous food; (*d*) abstinence from fluids; (*e*) uræmia; (*f*) cholera; (*g*) dysentery; (*h*) fevers; (*i*) acute and chronic parenchymatous nephritis; (*k*) formation of dropsical fluid; (*l*) in heart disease with diminished blood pressure; (*m*) obstructive suppression; (*n*) shock; &c.

Increase by :—

(*a*) Copious draughts of fluid; (*b*) cold; (*c*) much nitrogenous food; (*d*) diuretics—fluids charged with carbon di-oxide gas, milk-diet, &c.; (*e*) nervous excitement: hysteria; after an "epileptic fit;" (*f*) diabetes mellitus or insipidus; (*g*) "granular contracted kidney;" (*h*) "waxy kidney;" (*i*) convalescence from acute diseases; (*k*) absorption of dropsical fluid; (*l*) anæmia and chlorosis; &c.]

---

* In chronic interstitial nephritis, diabetes, and in cardiac disease with back-pressure, the night urine is markedly increased.

COLOUR.

Best judged by holding the urine up to the light when placed in a wide cylindrical glass vessel—*i.e.*, by "transmitted light." If the urine is not clear, it should be filtered before examining the colour.

Report according to Vogel's Scale,[*] here given.

A short method of recording the result is, for example, V. 5—*i.e.*, number 5 of Vogel's Scale (yellowish-red).

YELLOW.	REDDISH.	BROWN.
1. Pale yellow.	4. Reddish.	7. Brownish-red.
2. Light yellow.	5. Yellowish red.	8. Reddish-brown.
3. Yellow.	6. Red.	9. Brownish-black.

The *normal colour* ranges from straw-yellow to amber. Acid urines are darker than alkaline urines, even when of equal concentration. As a rule, women's urine is somewhat paler than men's. The urine's colour is normally deeper after active exercise and in warm weather,—from greater concentration.

When *pale or almost colourless* it indicates … Great dilution, which may be physiological or from hysteria, diabetes, granular kidney; or pallor may occur in anæmia, chlorosis, convalescence from acute disease, and in general debility.

---

[*] Vogel's scale is the only widely-known colour scale, and as such is recommended for use as affording some kind of standard for colour comparisons. It is, however, unsatisfactory, because its colours are meant to be observed by *reflected* light, while the best method of noting the colour of a urine is by *transmitted* light.

When *dark yellow* to *brown* it indicates	increased hæmolysis, as in fevers.
When *red* it indicates ...	large amounts of blood,[*] indican (indirubin being formed), or drugs such as rosaniline or (in acid urine) logwood, &c., or bilberries.
When *smoky* it indicates...	a small amount of blood.
When *brown to brownish-black* it indicates ...	Blood, carbolic acid, bile,[†] melanin from pigmented tumours.
When *greenish to brown* it indicates	Bile, salol, resorcin, juniper, carbolic acid, or much sugar (fermentation).
When *yellowish* (if urine is acid) *or* *reddish* it indicates (if urine is alkaline)	Drugs excreted as chrysophanic acid—*e.g.*, rhubarb, senna, &c.

Add an alkali if urine acid=becomes dark red.
Add an acid if urine alkaline=turns yellow.

When normal colour when passed but gradually becoming a deep brown colour (especially if alkali be added) it indicates ...	Alcaptonuria (from Dihydroxyphenyl acetic acid *which interferes with Fehling's test for sugar*). This may occur normally or when pyro-

---

[*] If urine is acid or if blood is present in small amount=smoky tinge. If urine is alkaline or if blood is present in large amount=reddish colour.

[†] Very deep coloured *bilious* urine on dilution with water becomes brownish-red or yellow. Such urine has a yellow froth.

	gallol and pyrocatechin (as in carboluria), hydroquinone, &c., are being excreted. Melanin also causes the same appearance (but does not reduce Fehling's solution). Uva ursi produces a like effect.
If *dark* and *muddy* (like porter) it indicates ...	Hæmoglobinuria or much altered blood.
When *dirty green or blue** it indicates	Indigogens (in putrefying urine in typhus and cholera). Methyleneblue may cause blue or green urine.
When *fluorescent* and *green* by reflected light and *pink* by transmitted light it indicates	Eosin or allied dyes in sweetmeats, spices, &c.
When *orange* it indicates ...	Santonin,† chrysophanic acid, or is occasionally due to bile.
When *whitish, opaque and jelly-like* it indicates ...	Chyle, or large quantities of pus.
When *reddish-yellow* soon becoming jelly-like it indicates	Fibrin.

---

* Logwood gives a *violet or blue* colour when excreted in alkaline urine; *red* when in acid urine.

† Santonin gives a purplish colour in alkaline urine and an orange colour in acid urine.

When *port wine colour* it indicates	Hæmatoporphyrinuria or Hæmoglobinuria.

ODOUR.—Normally, slightly aromatic and so characteristic as to be termed " urinous."

This urinous odour is much *increased* when the urine is much concentrated, or when urea is present in increased amount in the urine.

Ammoniacal or putrid odour	from fermentation; or from pus or blood.
Sweet (" new-mown hay " or whey-like) odour	in diabetes mellitus.
Chloroform-like odour ...	in acetonœmia.
Turned-milk like odour ...	when saccharine urine ferments.
Sweet violet odour	when turpentine is being exhibited.
Sweet briar odour	(rapidly becoming like that of rotten eggs) from cystin.
Characteristic odour ...	from garlic, cubebs, tolu, sandalwood, copaiba, asparagus.
Sickly odour	in dyspepsia.

REACTION is taken by red and blue litmus papers.* If alkalinity be due to ammonia, the paper turns red again *when dry.*

Normally, fresh urine is markedly acid (from Sodium Acid Phosphate, $Na\ H_2\ PO_4$). This is heightened during fasting (the so-called " acid tide ").

---

* N.B.—*Keep litmus papers in a well-corked bottle, as the blue papers especially become spoiled by exposure to air.*

But urine may normally be *neutral or even alkaline* after meals ("alkaline tide"), especially after a largely vegetable diet, particularly of potatoes—or when much fruit is being taken (effervescence will be caused by adding a mineral acid to such urine). The alkaline tide has generally set in about 1 hour after breakfast, and about 2 hours after dinner. The condition remains marked for about 1½ hours as a rule. It then gives place to the "acid tide," which lasts until the next meal is taken. The "acid tide" is proportional in strength to that of the "alkaline tide." Urine passed just before breakfast is normally more acid than at other times.

Diabetic urine is generally acid throughout the 24 hours—even at the time when the alkaline tide normally sets in.

Alkalinity, which is due to basic phosphates, and carbonates of Sodium, Potassium, and Ammonium (the last produced by the hydrolysis of urea during fermentation), may *normally* occur when the urine has stood for some time.

Diminished acidity occurs when the urine is much diluted; after repeated vomiting; after taking certain alkaline mineral waters and alkaline medicines; and after cold baths.

And *pathologically*, in Chronic Cystitis; in certain cases of dilatation of the stomach (especially after lavage); in old cases of urethral stricture where the bladder is not thoroughly emptied; in general debility, anæmia, defective liver action; by rapid absorption of alkaline exudations; and in certain spinal diseases.

The urine's *acidity is increased* from concentration—after active exercise, hot baths, fasting and fever. Also by leguminous or cereal foods (from their relatively high proportion of albuminous constituents); when the diet is largely composed of flesh or milk; administration of mineral acids, fluids charged with CO_2, benzoic acid.

Also in Fevers, especially acute Rheumatism; in acid dyspepsia; gout; chronic rheumatism; Diabetes mellitus.

Hyper-acid urines deposit urates on cooling, and generally, later, uric acid.

Urine after being passed goes on becoming increasingly acid up to a certain point, and then gradually becomes alkaline. The collected 24 hours' secretion has *generally* a markedly acid reaction, but may, even when normal, be neutral or alkaline.

Occasionally urine changes blue litmus red and *also* turns red litmus blue. This is the so-called *amphoteric reaction*, and is due to the presence of both acid and basic phosphates. It is of no known clinical significance.

(Though REACTION is a chemical change it is best considered here.)

SPECIFIC GRAVITY is taken in order to ascertain the average amount of solids eliminated. It therefore can only give reliable information when considered in relation to the quantity excreted during the 24 hours. It is most readily taken by the urinometer.

[The most accurate way, of course, is by the specific gravity flask, but this is impracticable for clinical purposes, not only as taking too long but also as requiring a chemical balance. The Westphal Balance may be used, but is not as convenient as the urinometer for rapid clinical work.]

Urinometers are generally graduated for use at the average temperature of the country in which they are made—*e.g.*, in England at 15.5° C. or 60° F. The urinometers of Squibb, of New York, are standardised at 77° F. (25° C.). In hot climates particularly it would certainly be much more accurate were samples of urine to be cooled to the temperature at which the urinometer is graduated.*

In an ordinary rapid clinical examination of the urine the custom is to allow the urine to cool to the temperature of the room, and then take the reading.

The following points must be carefully attended to when using the urinometer :—

(*a*.) Fill a clean, dry glass cylinder of two inches diameter about ⅔rds full with the urine. Pour the urine in gently so as to avoid frothing. Then allow to cool to the temperature of the room.†

---

* A new urinometer should always be tested to see if accurate at the temperature at which it is graduated. It should read 0 or 1000, when placed in distilled water at the temperature of graduation which is generally marked on the instrument.

† If the room's temperature is much above or below the temperature at which the urinometer is graduated *add* ·001 for every 3° Cent. *above*, or *deduct* ·001 for every 3° C. *below*, the temperature (Cent.) of graduation.

(*b.*) Dry the urinometer before placing it in the urine.

(*c.*) Float it gently in the centre of the cylinder. Take care that it floats clear of the foot and sides of the cylinder.

(*d.*) Remove any froth on the surface of the urine in the cylinder by means of blotting-paper.

(*e.*) When the instrument has come to rest, read the urinometer with the eye *on a level with the lower border of the "meniscus" or disc-like layer at the surface of the urine* where it cuts the urinometer's scale.

(*f.*) Compare the specific gravity with the total amount of the daily excretion.

A *miniature urinometer* may be used when the amount of urine is too small to render possible the employment of an ordinary urinometer.*

If the amount of urine be insufficient to allow of its specific gravity being taken by a urinometer, the following may be employed :—

(*a.*) The urine must be diluted with a sufficient amount of distilled water to cause the urinometer to float, carefully noting the volume of water added.

(*b.*) Then multiply the last two figures of the reading by the number of times the original volume of the urine has been increased. The result shows approximately the specific gravity of the undiluted urine.

Example.—If the urine has had three times its volume of water added (*i.e.*, if 4 volumes of fluid in all are being dealt with), then if the urinometer reading is, say, 1004, multiply the last two figures by 4, and the specific gravity is 1016.

---

* Messrs. Burroughs, Wellcome & Co., London, supply such instruments.

If the urinometer is inaccurately graduated, the error caused thereby will be heightened in proportion to the number of times the urine is diluted.

Specific Gravity beads may also be used, and are of two chief varieties:—

(*a.*) *Wilson's:* a set of beads with different numbers marked on them. The bead which *floats in the urine at any level* shows the specific gravity simply by reading its number.

(*b.*) *Oliver's* bead, which is marked 1008. Dilute the urine till the bead floats at any level, and then calculate according to the amount of dilution. (Wilson's beads are preferable as they save calculation.)

The average specific gravity in health is 1020, but ranges from 1015 to 1025. It may normally fall as low as 1002 (after copious drinking), or may rise to 1035 when the urine is very concentrated.*

Urea is the principal weight-giving constituent in *normal* urine, and then chlorides (albumin has no noteworthy effect on the specific gravity). Only substances *in solution* affect the specific gravity.

The largest proportion of solids occurs in the morning urine, and in that passed 3–4 hours after a meal. A full diet or exercise increases, and a low diet or sedentary life decreases the urinary solids. The urine of children under seven years of age yields relatively double the amount of solids that is excreted by people of eighteen years of age and upwards. After forty years of age, the solids gradually diminish in amount, even though the total quantity of urine may be normal or below normal. †

A high specific gravity may either be due to a high degree of concentration of the urine as after free sweating, vomiting, purging, at the commencement of fevers where it is due to an increased amount of urea, phosphates, and sulphates; or (with polyuria) in diabetes mellitus where the increased density is due to glucose and in part to urea (the latter being partly increased by the augmented proteid diet).

---

* During the first month of life the urine's specific gravity is 1001–05, but during the second year it rises to 1026–30.

† With ordinary diet and exercise a man of 145 lbs. weight should excrete about 35 grms. daily.

Between 40-60, deduct 10 °/o from this.
„ 60-70, „ 30 „ „
Over 70, „ 50 „ „

If the urine is copious, pale, and has sp. gr. over 1030, it strongly suggests the presence of sugar.

A low specific gravity is met with in many cachectic states, when there is sluggish liver action, and in general anæmia, and in conjunction with polyuria in diabetes insipidus, in nervous hydruria, in certain forms of heart disease, in acute nephritis (especially post-scarlatinal), renal hyperæmia, and where the amount of secreting renal tissue is lessened as in granular kidney, cystic disease, hydronephrosis, and certain other chronic forms of Bright's disease. In waxy kidney, however, the solids are often not diminished in amount, although the amount of urine is increased.

If the specific gravity remains persistently below 1010, it is necessary, in life assurance cases, to be specially on one's guard. A persistent low specific gravity (even without albuminuria) in people over forty should lead one to search carefully for tube-casts. In old age it is usually to be regarded as a grave indication of failure.

Lastly, it is well to bear in mind that a sudden fall in specific gravity in the course of Bright's disease, with no corresponding increase in the quantity of urine passed, often points to the early onset of uræmia.

TRANSPARENCY.—Normally urine is clear when passed, but a mucous cloud forms on standing, and, if concentrated, urates are deposited on cooling.

When urine is clear when passed, but becomes "thick" *later,* it points to...	Urates, Phosphates, Mucus, Decomposition.
If urine is "*thick*" *when passed,* it is suggestive of	Earthy Phosphates, Pus, Blood, Micro-organisms, Chyle, Bile, Mucus, Decomposition.

Normally, at the height of the "alkaline tide," the urine is milky when passed (due to the deficiency of acidity throwing the earthy phosphates out of solution).

When much mucus, pus, or chyle is present, it becomes thick and viscid, and, in fibrinuria, even *gelatinous.*

Small amounts of pus give a granular, whitish or greyish, hazy appearance, especially when the urine is held up to the light.

Opalescence is due to matters in suspension. A small amount of blood gives a *smoky appearance.*

Froth forms easily and lasts a long time on (*a*) highly albuminous, (*b*) or diabetic urines, and (*c*) when bile is present (froth is greenish-yellow).

Fluorescence may be present normally, but is specially frequent when the urine is ammoniacal.

If to fluorescent urine a dilute acid be added, ... = fluorescence disappears.
If an alkali then be added, ... = fluorescence reappears.

An iridescent pellicle due to phosphates is frequently observed, and is quite compatible with a healthy condition of the urine.

Urines containing a large proportion of urates often have a *bluish scum* on the surface.

Very small white flocculi in freshly passed urine, which are seen under the microscope to consist of leucocytes, point to gleet, and are often helpful in diagnosing latent gonorrhœa or gonorrhœal rheumatism.

See also section on the detection of gonococci.

DEPOSIT.—Set aside some of the urine in a covered cylindrical test-glass * for some hours.

[*If*, however, *it is desired to examine the sediment quickly*, a small centrifugal machine (such as Leffmann and Beam's, which is driven by hand, or one driven by electricity, such as Purdy's) may be employed. The urine is poured, as soon after being voided as possible, into strong test-tubes, which are then placed in the metal buckets of the centrifuge, which is then revolved for a few minutes when the deposit will separate, and the supernatant fluid can very readily be poured away from it.]

If the urine is not to be centrifugalised, then, while the sediment is separating, proceed with the chemical tests.

But be sure to note the reaction before setting it aside to settle.

Then return to the examination of the sediment, and note first its NAKED-EYE APPEARANCE.

White or grey, soft deposit with a sharply defined *undulating* upper surface, and with glittering particles here and there indicates *oxalate of lime and mucus.*

Ivory coloured deposit, with clear supernatant ACID *urine* indicates *pus.*

Whitish and ropy deposit, with thick supernatant ALKALINE urine indicates *pus* (generally from bladder, and accompanied by decomposition).

White deposit, with a thin film on surface, when urine is *neutral or alkaline,* indicates phosphates (Ca, Mg, Am-Mg).

Reddish-brown crystalline deposit (" cayenne-pepper grains"), usually slowly deposited from a markedly acid urine = *Uric Acid.*

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* Conical glasses are usually recommended, but are less easily kept clean nd the layers of deposit form less satisfactorily in them than in cylinders.

Chocolate-coloured or red deposit suggests blood, and clots may be present.

Light brown, pink or whitish deposit in concentrated, cold or markedly acid urine = acid urates (Na, K, Ca), or neutral calcium urate.

If the specific gravity is above normal, the deposit generally settles more slowly. If much mucus or albumin be present, pus subsides slowly, and *vice versâ.*

Most *unorganised* deposits may occur normally, so that it is more their quantity—whether excessive or not—than their mere presence which is of clinical interest.

[*Note.*—A deposit of Urates or of Phosphates does not necessarily point to excessive production and excretion, but may merely signify a slightly more acid or alkaline or concentrated condition of the urine which allows these substances to be more readily precipitated.]

The mucous cloud which normally separates from urine on standing shows under the microscope various forms of crystals, leucocytes, mucus corpuscles, and epithelium.

MICROSCOPIC EXAMINATION OF THE SEDIMENT.

To remove sediment for examination :—

(*a.*) Press the finger over the upper opening of a pipette.

(*b.*) Gently lower the nozzle *vertically* into the sediment, so that it lies *just over* the portion to be examined.

(*c.*) Ease the finger so as to allow the sediment to enter the pipette's nozzle.

(*d.*) Again press the finger tightly down, and remove the pipette.

(*e.*) Place a couple of drops on a clean glass-slide, and cover with a cover-slip.

Several slides ought to be examined with a high power (between 300 and 500 diameters) *from different layers of the deposit.*

Avoid using too bright illumination (by narrowing the microscope-diaphragm), otherwise the lighter coloured and more transparent substances in the sediment may be overlooked. Hence avoid using an Abbé's condenser altogether (except with oil-immersion lens for micro-organisms).

ORGANISED DEPOSITS.

BLOOD CORPUSCLES.—If the red cells are few in number, these may not affect the urine's colour. A moderate quantity causes a haziness or even a smoky appearance. If numerous they will colour the urine red.

A few isolated leucocytes are generally to be found in normal urines. In inflammatory conditions of the genito-urinary tract the amount is, of course, largely increased, and they may form aggregations (leucocyte casts), especially in acute nephritis. As leucocytes become pus-corpuscles in inflammatory processes there is difficulty in determining what is a leucocyte, and what a pus-cell. As a rule pus-cells show degenerative changes which leucocytes do not.

(*a.*) In *acid* urine, corpuscles generally have a normal appearance. *Red cells* (Erythrocytes)—round, biconcave, faint yellow, and remain unchanged for a fairly long time. *Leucocytes*—round, colourless, and markedly granular, with one or more nuclei.

(*b.*) In *alkaline* or dilute urine, corpuscles tend to swell up, and the red cells become pale and lose their biconcave shape. They are quickly disorganised by alkaline fermentation.

(*c.*) In *concentrated* urine, corpuscles tend to become small and crenated.

(*d.*) It is stated that rouleaux may be seen but this must be exceedingly rarely, and only in cases of profuse hæmorrhage.

The author has never seen rouleaux formed in urine. If they are met with it seems likely that it can only be in very free hæmorrhage from the anterior urethra in males or from the female genital tract.

PUS-CELLS form a yellowish-white, viscid deposit which becomes ropy and semi-solid in ammoniacal urine, and also when stirred up with Liquor Potassæ.

In *acid* urine, the pus as a rule is of renal origin.

In *alkaline* (especially ammoniacal) urine, the pus as a rule is of vesical origin.

Too much importance, however, must not be attached to the urine's reaction in judging of the source of pus. For example, as a general rule in slight pyelitis we have acid urine, and in well-developed cystitis an alkaline reaction.* But in pyelitis *accompanied by cystitis* the reaction may be alkaline. Alkaline urine has an irritating effect on the urinary passages, so that severe pyelitis tends to induce cystitis later.

In acid urine the pus-cells have a normal appearance —small, globular, markedly granular—and mostly lie separate from each other.

In alkaline urine, or if the specific gravity is low, the pus-cells swell, lose their outline, and become transparent and homogeneous with evident nuclei, which are brought out well by running a drop of 1 per cent acetic acid under the cover-glass. The cells often rupture and set free their nuclei. In very dilute urines the pus-cells may swell to twice or thrice their normal size, and might be mistaken for renal epithelium.

To distinguish pus-cells from epithelium—

Run a couple of drops of a solution of Iodine in Potassium Iodide under the cover glass—pus-cells (especially the nuclei) become brown—"glycogen reaction"—while epithelium stains a faint yellow.

Leucocytes (which are nearly always present in urine), lymphocytes, mucus or pus-corpuscles are practically indistinguishable microscopically.

Pus in marked quantity:

(*a.*) Causes traces of albumin in the urine.

(*b.*) The deposit becomes stringy on adding to it Liquor Potassæ (which dissolves up *mucus*).

See also Pus-casts.

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* In slight cystitis, especially at the beginning of the disease, the reaction of the urine may remain *acid*.

A good general rule for guidance is that when no trace of albumin is detectable the cells are not pus-corpuscles but normal leucocytes or mucus-corpuscles.

Any appreciable amount of pus would be accompanied by a proportionate amount of the albuminous *liquor puris*, or of nucleo-albumin derived from the pus-cells.

EPITHELIUM.—The point of most practical importance is the distinction of renal cells from those of the urinary passages and from swollen leucocytes.

Renal Epithelium—

(*a.*) Round, cubical, polyhedral or oval.

(*b.*) Sharp outline.

(*c.*) Relatively large, oval or round, single nucleus (thus distinguished from the polynuclear pus cells).

(*d.*) Frequently found adhering to fibrinous and other casts, or may form true epithelial casts.

But free cells may be so altered in size and shape and by degeneration by the action of an alkaline, fermenting urine as to be unrecognisable. The same remark equally applies to epithelium from the urinary passages.

Renal Pelvis and Ureter-Epithelium—

Flat and also generally tailed, oval, columnar, pear-shaped but may be round. The nucleus is relatively large.

Bladder-epithelium may closely resemble that from the renal-pelvis. Its form depends on the layer of the mucosa from which it is derived. Polyhedral or somewhat round cells come from the surface layer; tailed or pear-shaped from the middle layer, and oval, rounded or polygonal from the deepest stratum.

When the urine is alkaline, or especially if ammoniacal, it is often impossible to distinguish vesical epithelium as such.

Urethral Epithelium—Columnar, round, oval, spindleshaped, pear-shaped, or tailed, or cylindrical from males. In females the cells are more squamous, but smaller as a rule than vaginal or preputial squames. Round, oval, and slightly polygonal cells also may be derived from the female urethra.

Vaginal and Vulvar Epithelium—Irregular, polyhedral squames, often in groups. Transparent, granular, usually with one small nucleus. Outlines distinct. Cannot be distinguished certainly from epithelium from the male glans or prepuce. Bladder epithelium is generally somewhat thicker and less transparent than vaginal, but it is generally very difficult to be certain as to the source of squames.

The Mucous glands of the urinary passages may yield columnar, cubical or cylindrical cells.

CASTS.

I. ORGANISED.—Casts do not disappear readily in acid urines, but in alkaline urines are soon destroyed.

(*a.*) *Red Blood Cells.*—Casts composed of these occur especially *in acute nephritis* and renal hæmorrhage, and also in active and passive renal congestion. Such casts will often show that a hæmaturia is renal in origin.

(*b.*) *Leucocyte or Pus-casts.*—Such occur in glomerulo-nephritis, *suppurative-nephritis*, pyelo-nephritis.

(*c.*) *Epithelial Casts* occur in acute (especially post-scarlatinal) and chronic (parenchymatous) nephritis.

(*d.*) *Granular Casts* occur in acute and chronic (interstitial) nephritis, or in almost any variety of nephritis. These are often degenerated epithelial casts.

(*e.*) *Hyaline Casts.*—These may occur as a *transient* condition in renal hyperæmia, as after severe or prolonged exercise, in functional albuminurias, or in jaundice (in the last case often bile-stained). They occur in any form of nephritis, especially the interstitial and diffuse varieties; in waxy kidney, hæmaturia, passive renal congestion.

(*f.*) *Waxy or Colloid Casts* are *not* pathognomonic of waxy kidney, for they are hyaline or epithelial casts undergoing colloid degeneration, generally having been delayed in their passage from their point of origin. They occur in granular contracted kidney and other chronic renal inflammations, including the so-called waxy kidney.

They are distinguished from hyaline casts by being much broader, duller in colour, or yellowish, highly refractive, straighter, not transparent, less delicate in form, outline well defined.

Both hyaline and waxy casts are homogeneous in structure, and *non-striated* longitudinally. They may be convoluted and indented at the margins.

(*g.*) *Fatty Casts* are casts undergoing fatty degeneration. They are studded with droplets of fat of varying sizes. Epithelial casts are specially prone to fatty degeneration.

(*h.*) *Fibrin Casts* occur in hæmaturia.

They resemble granular casts, but are less regularly formed.

Casts may be found stained with bile, blood-pigment, by indican or other pigments occurring in urine.

THE PRESENCE OF CASTS does not afford certain proof of renal disease, *except in the case of purulent, blood, waxy, and, above all, of fatty casts.* The presence of fatty casts must, in general, be regarded as a sign of advanced organic renal disease—especially of chronic Bright's disease; but they are also found in poisoning by phosphorus, arsenic, antimony, &c.

Granular, epithelial, or an abundance of hyaline casts occurring in a person who has been kept quiet in bed for some time strongly suggests nephritis.

II. UNORGANISED CASTS.—

Urates (Ammonium urate casts in infants).

Hæmatoidin and pigment casts in hæmoglobinuria and in hæmaturia.

Granular Débris.

Melanin—in cachexias and melanotic cancer.

Calcareous—in cases of calculus: calcium carbonate casts disappear with effervescence when a drop of dilute mineral acid is run under the cover glass.

False Casts.—Uric acid, urates, phosphates, oxalates, may become deposited on mucous threads, and may simulate true casts which often have similar deposits. The ordinary solvents of these substances will disperse the deposits and show their true nature.

Mucous Casts or Cylindroids.—Another form of false casts which must be differentiated from true casts thus:—

(*a.*) *Outline*—indistinct, irregular, wavy.

(*b.*) *Diameter*—very variable at different portions.

(*c.*) *Ends*—tapered, frayed-out or split (never like true casts, with one end perhaps rounded, and the other end perhaps sharply broken off).

(*d.*) Under a high power, *longitudinal striation.*

(*e.*) *Do not dissolve in acetic acid* (unlike hyaline casts which they most resemble), but become less transparent and more highly granular.

(*f.*) Very long as a rule (much longer than hyaline casts which readily fracture. Usually, other varieties of true casts are short).

(*g.*) Are often seen to be sharply twisted and yet remain unbroken (unlike true casts which are very brittle).

Cylindroids may occur along with true casts, but are to be found in nearly all urines (normal or otherwise). They are increased in quantity in cystitis, urethritis, and other inflammatory conditions of the urinary tract.

Urethral and Gonorrheal "threads" occur especially in "gleet" and acute gonorrhœa. The threads consist of mucous filaments entangled with which are aggregations of leucocytes, gonococci, and often also erythrocytes, spermatozoa, altered blood pigment, &c.

Urethral (non-gonorrhœal) threads commonly occur in spermatorrhœa and sexual neurasthenia.

The morning urine should particularly be examined for "threads."

Spermatic Cylinders are casts from the prostatic ducts, and occur in chronic prostatitis, spermatorrhœa, and sexual neurasthenia. They are pale threads of homogeneous structure, longer and broader than hyaline casts, and not infrequently have spermatozoa embedded in them.

Spermatozoa.—These cannot certainly be identified from the head alone, and spermatozoa should never be pronounced present unless the conjoined head and tail are clearly made out. The presence of a few spermatozoa in urine is not of any clinical importance. They are normally present in the urine for some time after ejaculation. It is only when present more or less persistently in the urine, and in fairly large quantities that they become of importance. Spermatozoa rapidly lose their motility in alkaline urine, but otherwise retain their form for a long time as a rule (unless damaged by being shaken up).

[Seminal fluid in the urine, unless the quantity is minute, produces a *trace* of albumin.]

DETECTION OF GONOCOCCI
AND OF
TUBERCLE BACILLI IN THE URINE.

Only micro-organisms which produce tubercle and gonorrhœa can be considered in a work of this nature, as these are the only two organisms for which search is likely to be made under ordinary clinical conditions. The separation and detection of the other pathogenic germs found in the urine require an equipment of bacteriological apparatus and would occupy more time than the average practitioner could spare for the purpose.

THE GONOCOCCUS—

1. Is decolourised by Gram's method.
2. Occurs in colonies inside pus-cells (especially in the earlier stages of gonorrhœal infection).
3. Occurs also in gonorrhœal threads or sediment, and is especially abundant in acute gonorrhœa.

Method for Detection.

Allow the sediment several hours to separate, or centrifugalise, and then remove some of it with a pipette and stain and examine as follows :—

1. Place a drop on a cover-glass and then place a

second cover-glass on the drop and squeeze *very gently* together.

2. Separate the cover-glasses, place the wet sides uppermost, and allow to dry in the air.
3. Then stain for four minutes in Löffler's blue solution.*
4. Wash with distilled water.
5. Dry and mount.
6. Then examine *with a $\frac{1}{12}$th inch oil-immersion lens* (a lens of lower power is useless). Observe any oval cocci in pairs or (more rarely) in tetrads *lying within pus cells* (but not invading the nuclei). These diplococci are stained blue and look like two beans placed side by side, *with flattened or slightly concave adjacent margins*, the space between them remaining unstained. Frequently several groups of two—five, six, or more pairs—may be seen. Groups of two or four lying *outside* pus cells may be neglected.

GRAM'S METHOD should also be applied, as gonococci are decolourised thereby but pseudo-gonococci are not.

(*a.*) Take two other cover-glass preparations and stain for a quarter of an hour in a solution made by dissolving 30 c.c. of saturated alcoholic solution of Gentian Violet in 100 c.c. of anilin water. (3 c.c. of Anilin in 90 c.c. of water; shake; allow to settle and then filter.)

(*b.*) Then wash the cover-glasses in water.

(*c.*) Place for a couple of minutes in Gram's Iodine solution.†

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* *Löffler's blue solution* is prepared by mixing 30 c.c. of concentrated alcoholic solution of methylene blue in 100 c.c. of caustic potash solution (10 °/₀). Fixation with alcohol-ether is sometimes recommended but is superfluous.

† *Gram's Iodine solution:*

Iodine, 1 part; Potassic Iodide, 3 parts; Distilled water, 300 parts.

(*d.*) Remove and place in *absolute alcohol* till colour is discharged.

(*e.*) Then place for fifty seconds in Bismarck brown solution (a *saturated* watery solution is to be made and then diluted with thrice its bulk of water).

Note that the gonococci have no violet colour and are now stained brown only.

Especially in cases of chronic gonorrhœa in females the gonococci may frequently be present in such small numbers and so mixed with other organisms that the examination proves inconclusive. In such cases, and when few gonococci are present and these not contained in pus cells, cultures can alone decide the question, employing Wertheim's plate method.

TUBERCLE BACILLUS IN URINE.

Here the centrifuge is specially useful and should always be used, if possible; but where not available let the urine stand in a test-glass for some hours. It is a good plan to wash the centrifugalised sediment by shaking up with distilled water; and then re-centrifugalise.*

Make cover-glass "film" preparations and stain by Ziehl-Neelsen Carbol-Fuchsin Stain (Basic Fuchsin, 1 part; Absolute Alcohol, 10 parts; Carbolic acid, 1 in 20 solution, 100 parts).

Method.—

1. Place the cover-glass specimen in some of the stain placed in a watch-glass and *heat. From the time*

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* Where a centrifuge is not available, prepare films from the sediment, dry in air, place a few drops of distilled water on the film and heat gently over flame. Then stain exactly as above directed.

that steam begins to rise let it remain five minutes in the stain.

Take care not to overheat as the alcohol may take fire. Heat with a low flame or place the watch-glass high above the flame.

2. Place next in 20 per cent. sulphuric acid in order to decolourise.
3. Wash thoroughly with (distilled) water and if the film becomes markedly red place it again in the acid for half a minute or so and then remove, and wash *until it is a pale pink.*
4. Then place in saturated watery solution of Methylene Blue for half a minute in order to contrast stain.
5. Wash in water.*
6. Transfer the moist cover-glass to a slide and remove the surplus moisture with blotting paper.
7. Mount and examine.

The Tubercle bacilli alone will be stained red.†

The Smegma-bacillus (derivable from vulvar or preputial secretion) is practically the only difficulty likely to be encountered.‡ As a matter of fact, when the specimen is carefully made and well stained there is seldom any trouble on this score.

But if there is, prepare another specimen, and *after removing from the sulphuric acid*, dip the specimen for a few seconds into *absolute alcohol.* This will decolourise the smegma-bacillus, but not the tubercle bacillus.§

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* *If a permanent specimen is required.*—After washing the cover, allow to dry in the air; then pass through a flame in order to quite dry, and then mount in xylol balsam.

† The Leprosy bacillus reacts similarly.

‡ The smegma-bacillus is found in over 50 °/₀ of specimens of urine of females, but much less frequently in urine from males.

§ Inoculation of a susceptible animal is, of course, the surest method of all in cases of doubt.

Tubercle bacilli are often to be found in well-developed tuberculosis of the prostate, bladder, (testicle), and kidney, and very much more rarely in acute general tuberculosis. If a search for them is negative it by no means precludes the diagnosis of tuberculosis.

The urine is usually acid and albuminous in cases of local tuberculosis, but in advanced tuberculous bladder cases it becomes alkaline, as a rule.

PARASITES.—1. Micro-organisms,—putrefactive, sarcinæ (which have no pathological significance), pyogenic, pathogenic (typhoid, tubercle, gonorrhœa, relapsing-fever, erysipelas, ulcerative endo-carditis, &c.), or chromogenic. (For modes of separation and detection of micro-organisms other than Tubercle and gonococcus refer to works on Clinical Bacteriology.)

Micro-organisms,* when present in large quantities, cause a turbidity which on standing does not separate out as a sediment to any extent. This condition is commoner in women than in men as the female bladder is invaded much more readily on account of the shortness of the urethra.

2. WORMS, &c.

(*a.*) Embryos of Filaria sanguinis hominis;

In cases of chyluria (more especially when accompanied by marked hæmaturia) Filaria embryos are frequently to be observed in the urine.

(*b.*) Echinococci (hooklets, portions of cyst, scolices);

(*c.*) Ova of Distoma hæmatobium;

(*d.*) Ascaris lumbricoides (in recto-urinary fistula or from the rectum).

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* Normal urine is sterile.

UNORGANISED DEPOSITS

(Crystalline and Amorphous).

FROM ACID URINE.

AMORPHOUS :—

Urates of Potassium, Sodium and Calcium.

CRYSTALLINE :—

(*a.*) Uric Acid or Urates;
(*b.*) Calcium Oxalate;
(*c.*) Leucin;
(*d.*) Tyrosin;
(*e.*) Cholesterin; } rare.
(*f.*) Cystin;
(*g.*) Hippuric Acid;
(*h.*) Calcium Carbonate and Sulphate (very rare).
(*i.*) Di-acid Calcium phosphate (very rare).
(*k.*) Hæmatoidin or Bilirubin.

FROM ALKALINE URINE.

AMORPHOUS :—

Tri-calcic Phosphate.
Calcium Carbonate (rare).

CRYSTALLINE :—

(*a.*) *Acid Ammonium* urate;
(*b.*) Phosphates of Calcium, Neutral Magnesium (rare), and Ammonio-Magnesium ("Triple phosphate").
(*c.*) Leucin and Tyrosin (very rare; nearly always occur in *acid* urines).

In feebly acid urine beginning to turn Alkaline—

Acid Calcium (rare)
Basic Magnesium (rare) } Phosphates.
Ammonio-Magnesium

UNORGANISED DEPOSITS.

URATES occur as Urate of Sodium, Potassium, Calcium, Ammonium, and Magnesium. Urates separate from acid urines of high specific gravity as a brick-red or grey sediment.

The separation of urates may occur on the cooling of the urine, but not infrequently the separation is delayed for some hours after cooling, until the urine has become more markedly acid. (Calcium Oxalate very frequently occurs along with urates.)

Amorphous urates are chiefly those of sodium, potassium, and calcium. They occur *in acid urines* (often along with uric acid), and vary in colour from brownish-red to faint pink* or *grey*. Under the microscope they form a series of faintly coloured grains—much smaller than in the case of amorphous phosphates—and only when aggregated display the colour of the deposit as seen by the naked eye.

Sodium biurate, or acid sodium urate occurs along with the foregoing in acid urines of high specific gravity. It may form a *brick-dust* ("lateritious") or sandy deposit, easily soluble on heating; or may be pink, brownish, yellow, or grey. This substance appears as an *amorphous* deposit, also as round balls, with projecting hooks or spikes; and also as "hedge-hog forms," and stars, and rarely as rosettes and sheaves. In gout and rheumatism this (as well as sodium quadriurate) is much increased in amount in the urine.

Calcium urate occurs in acid urines as an amorphous or crystalline deposit—as colourless, amorphous grains or as stars or balls composed of long needles, which latter also occur separately. It is soluble on heating only to a slight degree.

Acid ammonium urate is nearly always deposited by *alkaline* (*especially ammoniacal*) urines, and, therefore, often occurs along with phosphates. It forms brownish or yellowish spiky spheres, rhizomes or stars, and also occurs as almost colourless needles, often in star-like groups or sheaves. It is also found as casts in new-born children, and in calculi in children.

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* The pink or reddish colour is due to a pigment of great colouring power called Uroerythrin. This pinkish deposit consists largely of sodium quadriurate.

It gives the murexide reaction in common with the urates of Potassium, Sodium, Magnesium, and Calcium.

URIC ACID occurs much less frequently than urates as a deposit. It is generally thrown out of solution by concentrated *acid* urines *on cooling* and by *increase of acidity on standing.* It is more often from dark coloured concentrated urines that urates and uric acid separate, but urines with a low specific gravity may also deposit these substances.

A high degree of acidity, a relatively small proportion of mineral salts and pigments, and a large amount of uric acid are, according to Sir William Roberts, the chief factors which cause *rapid* precipitation of uric acid.

Again, the degree of acidity of the urine, and the relative proportions of pigments and other substances present, modify the *shape* of the crystals of uric acid. With slightly acid urines the ordinary yellow or brownish *rhombic*, dumb-bell, lozenge, cruciform, star, whetstone, and barrel-shaped crystals occur, while in hyper-acid urines, the lance-head and other unusual forms are found.

Colourless uric acid crystals principally occur in leukæmia, in very dilute urines, and in urines undergoing ammoniacal fermentation.

Xanthin also occurs as colourless whetstone crystals, and may be distinguished from uric acid by giving the Xanthin reaction (see p. 47). It is exceedingly rarely found as a urinary deposit.

To the naked-eye the "cayenne-pepper grains" of uric acid are frequently to be observed. They are found towards the surface of the deposit, or intermingled with a uratic sediment.

Uric acid crystals may be coloured variously by pigments occurring in the urine—greenish or dark brown from bile, blue from indican, or by various drugs—*e.g.*, carbolic acid, salicylates, &c.

Clinical significance of sediments composed of urates and uric acid. It is to be particularly noted that a deposit of urates is not by any means to be regarded *as indicating increased production or excretion.* Such deposits result, in many cases, merely from increased acidity or concentration of the urine. When persistently present in large amounts they may point to excessive tissue waste as in fevers, diabetes,* pernicious anæmia, or severe organic disease. In the uric acid diathesis, acute rheumatism, and where uric acid or uratic calculi are being formed, urates are much increased in amount, and uric acid may be freely deposited. (See also p. 138.) If *uric acid* is deposited *from freshly voided urine or on cooling* it is generally of pathological significance.

Uric acid and URATES may be detected by the MUREXIDE TEST :—

(*a.*) Add a few drops of HNO_3 to *some of the concentrated urine* or deposit.

(*b.*) Then evaporate to dryness in a porcelain capsule = yellowish-red residue (alloxantin).

(*c.*) Add a few drops of ammonia solution = violet colour (ammonium purpurate).

Or to another portion of residue add a couple of drops of caustic potash or soda = dark blue colour, which disappears on heating.

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* Uric acid often precedes, or alternates with, glucose in Diabetes.

PHOSPHATES.

The most common whitish or greyish deposits are those caused by pus, "pale urates" and phosphates. Caustic potash, heat and mineral acids readily distinguish these from one another (see p. 50).

The Earthy Phosphates (calcium much commoner than magnesium) are those which occur most frequently in the sediment—mostly in alkaline, rarely in neutral and very occasionally in faintly acid urines. They occur chiefly as colourless amorphous granules often along with crystalline phosphates. They do *not* dissolve on being heated (as do urates), but dissolve without effervescence upon adding a drop of nitric or acetic acid. Ammoniacal urines generally deposit earthy (amorphous and triple) phosphates.

Tri-Calcic Phosphate [$Ca_3 (PO_4)_2$] is amorphous and specially occurs in alkaline urines.

Acid Calcium Phosphate ($Ca\,HPO_4$) commonly occurs as large crystalline prisms, and forms the so-called *stellar phosphates—i.e.*, prisms arranged as stars; but also forms fans and sheaves; and also dumb-bells and globular masses. It is found in faintly alkaline or acid* or neutral urines. (This form is frequently but erroneously termed "neutral" phosphates.)

Crystals of Di-acid Calcic Phosphate are very seldom encountered. They occur in *hyper-acid*, concentrated urines.

Ammonio-Magnesium Phosphate, or "triple phosphate," is one of the commonest forms, and occurs in alkaline (especially ammoniacal) urines,—and occasionally in faintly acid urines. The colourless knife-rest and "coffin-lid" "forms" and stars with serrated edges are the commoner types of crystals. Feathery stars are rarer.

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* The deposit of stellar or acid phosphates from acid urine is often accompanied by symptoms which have led to the term "phosphatic diabetes" being applied to this condition. Saccharine diabetes not infrequently supervenes.

Neutral Magnesium Phosphate is a rare form occurring in alkaline, concentrated urines.

It occurs as long colourless rhomboidal plates with square-cut or oblique ends, or as irregular-edged squames. Golding Bird has pointed out that these crystals specially occur in cases of dilated stomach.

[*The Alkaline Phosphates* (potassium and acid sodium) are very soluble salts, and are not found as deposits. Unlike the foregoing, they are *not* precipitated by alkalies. They are only detected by first eliminating the earthy phosphates (add caustic potash, heat, filter off earthy phosphates), and then treating the filtrate with a solution composed of equal parts of magnesium sulphate, ammonium chloride, and ammonia solution to 8 parts of water. This will give a *white* precipitate with alkaline phosphates.]

PHOSPHATURIA.—Like urates, the presence of phosphates may be of no clinical importance.

The earthy phosphates separate out readily from deficiently acid, and from neutral or alkaline urines. Thus they may occur as deposits during the "alkaline tide," and as the result of partaking of a largely vegetable diet, or when alkaline drugs or mineral waters are being taken. But the earthy phosphates are found actually *increased* in osteomalacia, rickets, and certain central nervous diseases, and are *diminished* as a rule in pronounced renal disease. In cystitis, phosphates (particularly "amorphous" and "triple") are found in association with pus.

Phosphates and oxalates frequently occur in the same specimen.

It is, therefore, never the presence of phosphates, even in large amount, that should lead to a diagnosis of the so-called phosphaturia or "Phosphatic Diathesis." Any opinion to this effect should be based on *quantitative* estimations of the phosphates in the 24 hours' collected urine. This is rendered specially necessary from the fact that *a considerably increased excretion of phosphates may be taking place without any sedimentation resulting.* This may result from the acid reaction of a urine being favourable to solution of phosphates or from the predominance of highly soluble phosphates (such as the alkaline) which alkalinity of the urine does not cause to be precipitated.

Calcium Sulphate is very rarely found, and then in *acid* urines as colourless, blunt-pointed, needle-shaped crystals often arranged as stars.

Calcium Carbonate is relatively of rare occurrence. It is usually found in *alkaline* urines, generally along with phosphates. It occurs as an amorphous deposit or as colourless, crystalline, concentrically-striated balls, crosses, dumb-bells or rosettes. If a drop of nitric acid be run under the cover-glass, the deposit dissolves *with effervescence.*

CALCIUM OXALATE often does not separate for some hours, and so may be missed. It is a light-coloured deposit, generally crystallising in fine glistening lines on the sides and foot of the vessel.

It occurs in acid urine ordinarily as colourless, glistening, transparent, octahedral or "envelope" crystals, varying greatly in size. The round or oval forms are found much more rarely, and if seen lying on edge have a dumb-bell or hour-glass appearance. A marked amount of mucus generally accompanies the deposit. Oxalates occasionally replace sugar in cases of diabetes mellitus. This temporary disappearance of sugar and alternation with oxalates or uric acid is comparatively rare.

Oxalates occur in urinary deposits chiefly as Calcium Oxalate as Sodium and Ammonium Oxalates are much more soluble salts. *They are insoluble in acetic acid* (distinguished thus from carbonates or phosphates) *or in ammonia* (unlike urates).

Oxaluria is diagnosed by the persistence of relatively large amounts of oxalates in the urine, and this should be *quantitatively* ascertained. Irritation of the kidneys,* bladder and urinary passages often accompanies this condition. It occurs specially in men between the ages of eighteen and thirty, as the result of dietetic errors (eating rhubarb frequently causes it in some people—also onions and tomatoes), sedentary habits, or very often from overstrain or mental anxiety. It also occurs after severe burns and in convulsive nervous affections—epilepsy, tetanus, and also in delirium tremens and cerebral apoplexy.

Cholesterin is of exceedingly rare occurrence. The flat, thin rhomboids are colourless or slightly yellow-tinged, and have one or more corners squarely cut out, or stepped. It occurs in acid (or faintly alkaline) urines, in fatty degeneration or waxy disease of the kidney, in cystic or hydatid kidney disease, and in lipuria.

Cystin is observed rarely, and then in *acid* urine. It occurs as colourless, thin, six-sided crystalline plates—often super-imposed in layers as well as lying singly. They are insoluble in acetic acid, but dissolve on adding ammonia. When present in marked amount, suspect a calculus. It also occurs, however, in struma and in certain liver diseases. *Traces* of Cystin may normally occur in urine.

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* Oxaluria may occasion temporary albuminuria.

XANTHIN is very seldom found as a urinary deposit, and it then forms minute colourless lemon-shaped or "*whetstone*" crystals. It occurs especially in young people, and as an ingredient of certain forms of calculi.

It is deposited from acid urines, and is soluble in distinctly alkaline urines.

Xanthin reaction:—If some of the residue is treated with a few drops of strong HNO_3 and slowly evaporated to dryness = bright yellow residue. Allow to cool and then touch the residue with liquor potassæ = *dark red colour* (Hypo-xanthin gives an orange colour when similarly treated).

Colourless "whetstone" crystals of uric acid may readily be mistaken for Xanthin. The above-mentioned Xanthin reaction will not certainly distinguish between the two. For, in the presence of chlorides, the Xanthin crystals will respond to the Murexide reaction as well as uric acid. (Xanthin, Hypoxanthin and Uric Acid are closely allied chemically, and the two former occur in normal urine.)

LEUCIN AND TYROSIN occur together and take the place of urea in Acute Yellow Atrophy of the liver, in phosphorus poisoning, pernicious anæmia, and occasionally in variola and typhoid fever, and in fluid from hydronephrotic cysts.

In examining for these substances, first evaporate the urine to a thin syrupy consistence.

Leucin occurs as yellow or light brown, oily-looking balls with concentric and radial striation (due to radiating crystals). They resemble balls of acid ammonium urate, which, however, have spikes at the margin, are smaller, and are not striated. It is much more soluble than Tyrosin.

Tyrosin crystals usually occur in the same specimen, but much more abundantly than Leucin, being less soluble than it and hence more easily precipitated. They are needle-shaped crystals, and are arranged generally in stars, sheaves or fans. They may have a colour similar to leucin, or may be greenish, or may again be colourless. They dissolve in ammonia but not readily in acetic acid.

HIPPURIC ACID is another very rare deposit of no known clinical significance. It occurs as colourless, narrow, flat rhombic crystals, with sharp ends. It is found in hepatic diseases, and occasionally in diabetes mellitus and fevers. Normally it occurs in small amounts as hippurates but it may be found in relatively large amount when fruits containing much benzoic acid (bilberries, plums, cranberries, blackberries, pears) are taken, and after administration of salicylates.

Urea Nitrate never occurs as a spontaneous deposit in urine. It may be found in concentrated urine to which strong nitric acid has been added in testing for albumin. In such cases it forms a shining crystalline deposit, as a rule slowly formed.

It is often of importance to detect the presence of urine in certain fluids, and this is generally done by ascertaining the presence of urea (or uric acid by the murexide test). The fluid is concentrated to a syrupy consistence on a water bath, and strong nitric acid is then added, and any resulting deposit is examined under the microscope.

Or, again, three or four drops of the fluid may be placed on a microscope slide and concentrated over the flame of a spirit-lamp until a white ring forms at the margin. Then cool and add two drops of strong nitric acid. Put on a cover glass and examine particularly the periphery for urea nitrate crystals (see Plate).

HÆMATOIDIN OR BILIRUBIN present exactly similar appearances, and may occur as yellow amorphous grains or as yellow or brownish-red, sharp, slender, separate needles or stars; or (less commonly) as rhombic plates. The deposit responds to Gmelin's test, and dissolves in acetic or a mineral acid, or in an alkali. It *occurs in* acute nephritis, hæmaturia, cancer of the bladder or liver, jaundice, acute yellow atrophy of the liver, or in abscess of the kidney or urinary tract.

FOREIGN SUBSTANCES.

Fat globules, starch granules, lycopodium spores, iodoform, crystals of other substances used in urethral or vaginal medication; yeast-cells; moulds; hairs; cotton, silk, wool or linen fibres; very occasionally fragments of tumours (Carcinoma, Sarcoma, fibroids, &c.). In cases of fæcal fistula, or where particles of fæces have found their way into the urine, undigested vegetable- and muscle-fibres may be observed.

For Illustrations of Urinary Deposits, see plates at the end of the book.

QUALITATIVE CHEMICAL EXAMINATION.

IF TURBIDITY BE PRESENT, *heat* a small amount of urine in a test-tube.

(*a.*) If it clears up = URATES.

(*b.*) If not, add two or three drops of nitric acid, and if it clears = OXALATES OR PHOSPHATES (to distinguish, add to a fresh portion of urine some ammonia = ppt. Then add a few drops acetic acid. If ppt. dissolves = *Phosphates.* If it does not dissolve = *Oxalates*).

(*c.*) If, on adding nitric acid, it clears with effervescence = CARBONATES.*

(*d.*) *If still it does not clear*, add a little liquor potassæ. If it clears = MUCUS. If it becomes difficult to pour and glairy = PUS.

(*e.*) If neither heat nor acid clears it = MICRO-ORGANISMS.

(*f.*) If heat and acid increase the turbidity = suspect ALBUMIN, for which now test.

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* When the HNO_3 contains nitrous acid, urea or urates may be decomposed with effervescence.

ALBUMIN.

Urinary proteids may, for clinical purposes, be classed thus:—

- I. The Natural Proteids of the Blood (coagulated by boiling),
  - *Serum albumin* (commonest and most important of all).
  - *Globulin* (next in frequency of occurrence).
- II. Derived Proteids (either do not coagulate with heat or redissolve before boiling-point), .
  - *Albumoses* (rare).
  - *Acid-albumin* (may occur as such when the urine is hyperacid — *e.g.*, when mineral acids are being administered).
  - *Alkali-albumin* (may occur in alkaline urines).
  - *Peptones* (occurrence very doubtful).
- III.
  - *Mucin*, ... } Might be mistaken for true albumin.*
  - *Nucleo-albumins*, . . . }
  - *Fibrin* (occurs rarely, and is readily detected by microscope and by separate tests).

Having regard to the great importance of being able to pronounce definitely as to the presence or absence of albuminuria, the safest plan is to apply all three of the following tests:—(1) Heat; (2) Nitric Acid; (3) Picric Acid. This is specially necessary when negative results or indications of only traces of albumin are being obtained. *Where a relatively large amount of albumin is present, however, the results obtained with the heat and nitric acid tests are so unmistakable that it is generally unnecessary to confirm the result by the picric acid test also.*

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* Albuminuria is the term applied to the occurrence in the urine of serum-albumin and globulin in particular (and also of acid or alkali-albumins). Albumosuria, peptonuria, mucinuria, fibrinuria, and nucleo-albuminuria designate the occurrence of the other proteids, as distinguished from true albuminuria.

The above-mentioned three tests are by far the simplest, most rapid, and most reliable of all albumin tests. They may be depended on to show the faintest pathological trace of albumin. The author's reason for advocating the employment of all three tests as a matter of routine is not only for confirmatory purposes, but in order that possible fallacies, incident to any single test, may be avoided.*

THE HEAT TEST, *in acid urines,* shows the presence of *serum albumin* and *globulin.*†

THE NITRIC ACID TEST confirms the indications of the heat test and further *detects mucin* ‡ (which the heat test fails to do). In fact, this acid precipitates all the urinary proteids (except peptones, the occurrence of which in urine is open to much doubt). *Hetero-albumose* is by this test distinguished from all others as its ppt. dissolves on heating and reappears on cooling.

THE PICRIC ACID TEST further confirms the presence of serum albumin and globulin even in the form of acid- or alkali-albumins (Sir George Johnson); detects *deutero-albumose* (and peptones); and gives no ppt. with mucin, thus helping to distinguish this group of proteids from albumin. It is a more delicate test than either of the others, though the heat and nitric acid tests will readily detect 0·002 per cent. of albumin.

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* Where a PORTABLE *reagent for albumin* is required, employ preferably salicyl-sulphonic acid (*see* p. 66), or picric acid. Both can be conveniently carried as finely powdered crystals and, in addition, all that is needed for the test are a small test-tube, litmus and filter papers, and a lamp. Salicyl-sulphonic acid is also non-corrosive. But for tests applied at home or in hospital, apply the heat, nitric, and picric acid tests.

† The readiness with which albumin is precipitated partly depends on the presence of other dissolved matters—*e.g.*, certain neutral salts, for the solubility of proteids turns on the relative amount present of these as well as on the reaction and temperature of the solvent fluid. Serum-albumin and globulin coagulate at about 75° C., and this occurs more readily if neutral salts are, relatively, present in excess.

‡ *Nucleo-albumins* (which are frequently included under the general term mucin but from which they are quite distinct) react to all the tests for serum albumin *except the heat test.* Mucin also gives no reaction with the heat test.

DETECTION OF ALBUMIN.

HEAT TEST.

I. *Filter the urine in every case.*

This is necessary to remove mucus, blood-cells, spermatozoa, pus, &c., and it is essential to test a clear and transparent portion of the urine, or else traces of albumin may be missed. Filter through a small funnel into a test-tube.

Where the urine is turbid from micro-organisms, filtration will not clear it sufficiently. In such cases, shake up the urine, either with finely powdered barium carbonate or with infusorial earth (Kieselgühr), and then filter.

II. If the reaction has not been taken previously, take it now.

If acid, proceed with tests.

If alkaline, add cautiously, drop by drop,* dilute acetic acid (2 per cent.) till the urine sharply reddens a piece of blue litmus paper. (*Shake up after each addition of the acid.*)

III. Half-fill a test-tube with the filtered urine (acidified if necessary), and heat *the upper layer of liquid* † in a spirit-lamp or Bunsen flame.

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* (*a*) Caution is necessary as, if *too much* acetic acid be added, an acetate of albumin forms *which heat does not coagulate*. One or two drops of *dilute* acetic acid ordinarily suffice.

(*b*) *When a cloudiness or ppt. results on adding dilute acetic acid* [and when, later, the HNO_3 test gives a more typical reaction *after dilution of the urine with an equal bulk of water* than with the undiluted urine], it indicates mucin or nucleo-albumin, *which see*.

† This is préferable to heating the whole length of the column of urine in the tube, as *traces* are much more readily detected when the upper layer of urine alone is heated. Further, it has the great advantage of enabling one to compare the heated layers at the upper part of the tube with the cold layer at the foot—*e.g.*, when urates and albumin are both present we may get an albumin

If albumin is present a white cloud will form at the surface and this will spread downwards, settling later as a soft, white, flocculent, opaque precipitate.

If a large amount of albumin be present the whole column of urine will coagulate.

Where only traces of albumin are present hold the test-tube against a black surface in order to intensify any haziness.

If *phosphates* be present the cloudiness occurs *later* than with albumin—just before boiling.

To distinguish, add strong nitric acid, drop by drop (not more than $\frac{1}{10}$th of the urine's volume)—one or two drops generally suffice.

If the cloudiness entirely clears up = *phosphates.*

If the cloudiness or ppt. is *increased* on adding HNO_3 = *albumin.*

Cautions as regards the Heat Test :—

I. *If the urine is* ALKALINE *no ppt. occurs on heating.*

II. If the urine be excessively *acid* the *albumin may not be precipitated by heat* (as an acid albuminate may be formed and this is not pptd. by heat).*

III. If *too much* HNO_3 be added, and if there be a comparatively small amount of albumin present, the acid may dissolve it up again as a nitrate of albumin, or acid albuminate. Further addition of HNO_3 will coagulate this but heating will not.

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cloud in the uppermost layer of urine, then next a clear layer due to the urates having dissolved on being heated, and at the foot of the tube the cold turbid urine.

* Acid and alkali-albumins are pptd. on careful neutralisation of the urine, and these ppts. re-dissolve on further addition of alkali or acid.

IV. If, on the other hand, phosphates *also* are present and *too little* HNO_3 be added the albumin may form a soluble albuminate with the phosphates and so escape detection if the amount of albumin is small.

V. If a cloud comes on heating *which clears up before the boiling point = hetero-albumose.* If cloud lessens but does not clear up = *albumin and albumose.*

VI. Uric acid may be pptd. by nitric acid but this—
(*a*) is a brown and non-flocculent ppt.;
(*b*) does not separate until the urine has cooled;
(*c*) redissolves on heating again.

VII. Copaiba resins are pptd. by heat but are distinguished from albumin by dissolving on addition of *alcohol.*

[When the ppt. is allowed to settle for 18 or 24 hours, a very rough approximate idea may be formed as to the *quantity* present—*e.g.*, one-third or one-fourth the total bulk of urine taken, but see p. 109.]

COLD NITRIC ACID TEST (HELLER'S TEST).

(*a.*) Place about half-a-drachm of strong nitric acid in a test-tube.

(*b.*) Then tilt the test-tube considerably, and *gently and slowly* pour down the side about an equal volume of the filtered urine; and slowly

(*c.*) restore to the vertical position.

If albumin is present a disc-shaped, white, flocculent ppt. forms at the plane of contact of the two fluids.*

If much albumin = an immediate coagulum.

If *traces* only = a cloudiness or ppt. forms in from 5 to 15 minutes at the junction of acid and urine.

Where only a very small quantity of urine is available for testing for albumin, draw up a few drops in a small pipette, and then draw up some strong HNO_3 = zonular ppt. at junction of fluids if any albumin be present.

CAUTIONS IN EMPLOYING THE HNO_3 TEST.

1. Mucin forms *a diffused haze* (not like albumin, an opaque disc) towards the upper surface of the urine. † On heating, the haze does *not* disappear.

2. Hetero-albumose gives a white opacity often also towards the surface. Distinguished from Albumin or Mucin by *disappearing on being boiled, and reappearing on cooling.* (The opacity also disappears on adding excess of HNO_3. So in testing for *albumose* add the acid drop by drop.)

3. Both Nucleo-albumin and Mucin may give with HNO_3 test a faint indistinct reaction *occurring after some time.* Take a fresh portion of urine, dilute with an equal bulk of water, and repeat the HNO_3 test. If there is a more pronounced reaction than with the undiluted specimen it indicates Mucin or Nucleo-albumin.‡

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* If HNO_3 be poured into urine rapidly or in great excess, acid albumin may be produced, or a small amount of albumin may be dissolved up. No ppt. will then result, and in this way the presence of albumin may be overlooked. This cannot occur if the test is applied as above directed.

† Mucin dissolves in strong HNO_3, but is ppd. by dilute acid as towards the upper surface of the urine in the above test.

‡ *Large amounts* of nucleo-albumin react like serum-globulin or albumin with HNO_3 and picric acid. *The heat-test, however, gives a negative result, thus distinguishing nucleo-albumin or mucin from true albumin.*

4. Uric Acid, urates and urea nitrate may form a crystalline layer with the HNO_3 test. These can be distinguished by *repeating the test with urine diluted with an equal bulk of water*, when no such layer results. Further, the uric acid layer is very ill-defined, and *dissolves on heating;* and nitrate of urea forms, *very slowly*, crystalline flakes—often above the plane of contact—which if examined microscopically have a typical appearance (see plate).

5. Turpentine, Sandalwood, Copaiba, Styrax, and other resins give a diffused haze which—

(*a*) clears up on heating;

(*b*) or on adding an equal volume of either rectified spirit or ether.

(*c*) The odour of the urine and history of the case will also help.

6. Fatty acids also give a haze which, however, dissolves up on adding an equal bulk of ether.

7. A reddish-violet or ruby-coloured ring above the nitric acid layer is derived from oxidation of the normally present urinary indigogens (these are increased in amount in fevers, chronic constipation, or in intestinal obstruction). In anæmia with pale coloured urine there is frequently to be observed a purple colour on adding HNO_3. Hold the test-tube up to the light and such bands are seen to be transparent, unlike an albumin cloud.

Note.—When iodides or bromides are being administered, the urine may turn a dark colour on adding nitric acid. This is due to the liberation of free iodine or bromine which may be recognised by their odours, or by shaking up the urine with some chloroform, which is then separated and gently evaporated, and the residue tested for iodine or bromine.

8. Albumin coagulum may be coloured from the presence of normal or abnormal pigments.

9. Effervescence on adding HNO_3 is often caused by carbonates or by decomposition of urea or urates with evolution of nitrogen and CO_2. This latter occurs when the HNO_3 contains some nitrous acid.

PICRIC ACID TEST.

To one inch depth of the filtered urine in a test-tube Picric Acid (*either about ½ grain of finely powdered crystals or a saturated aqueous solution*)* is added and gives an immediate *yellowish-white flocculent turbidity*, if even faint traces of albumin are present.

Now gently *heat* and the *turbidity is increased*. (Take care not to overheat the solution.)

No other acid—e.g., acetic, should have been added to the urine before adding the Picric Acid.

For the Picric Acid test the urine should be quite clear.

CAUTIONS IN EMPLOYING THE PICRIC ACID TEST.

(*a.*) In *strongly* alkaline urine, the albumin will not respond to the Picric Acid Test as the picrate of albumin which forms is soluble in a strongly alkaline medium. But if the urine is *neutral or only slightly alkaline*, the Picric Acid is sufficiently strongly acid to prevent this occurrence, and also to dissolve up any phosphates present.

(*b.*) Where much albumin is present the turbidity caused by adding Picric Acid may disappear on shaking. Add some more Picric Acid and the turbidity reappears and remains permanently. The ppt. produced by Picric Acid is not dissolved up by adding excess of that reagent.

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* A saturated solution is 7 grains of Picric Acid to 1 oz. of water.

(*c.*) Deutero-Albumose (Peptones) or a large excess of Urates, or Piperazine, Creatinin, and Alkaloids such as Quinine, Antipyrin, &c., are also pptd. by Picric Acid. Such ppts. *dissolve on heating.*[*]

If albumin be also present, the ppt. with Picric Acid *diminishes* but does not disappear on heating. *If albumin and albumose occur together*, filter while hot = pptd. albumin remains behind on the filter paper. The filtrate becomes cloudy or gives a ppt. on cooling (albumose).[†]

Mucin is NOT PPTD. by Picric Acid, but nucleo-albumin is ppd.

The following additional test is given as perhaps being the most delicate of all albumin tests :—

TANRETS MERCURIC-POTASSIUM IODIDE TEST.

The *reagent is prepared* by dissolving 1.35 grammes of mercuric chloride, and 3.32 grammes of Potassic Iodide in 64 c.c. of water, and then 20 c.c. of strong Acetic Acid are added.

(*a.*) Unless the filtered urine is fresh and acid, add a few drops of Acetic Acid to detect and precipitate Mucin, which should be filtered off ;

(*b.*) Then add a few drops of the reagent = white flocculent ppt. or opacity ;

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[*] Citric Acid is often used along with the Picric Acid with the object of keeping phosphates in solution, but is an unnecessary adjunct to the test.

[†] Picric Acid followed by the addition of a drop of dilute Liquor Potassæ gives a *deep red colour* with Creatinin or Acetone (less intense with Acetone). Glucose gives the same reaction *on heating.*

(*c.*) Heat gently = ppt. or opacity remains if only albumin be present.

Cautions—1. Deutero-albumose (peptones), urates, uric acid, and alkaloids may be pptd., but are distinguished from albumin by dissolving when gently heated. The ppt. or opacity only lessens, but does not disappear, if albumin, *plus* any of the above, is present.

2. Bile salts may also give a ppt. with this test, but are dissolved on adding ether.

3. Mucin is also precipitated, but, if the tests have been carried out as directed above, it would have been distinguished and eliminated.

[Other tests—*e.g.*, Potassium ferrocyanide with acetic acid, trichloracetic acid, Millons' reagent (mercuric nitrate), &c., are superfluous and, in general, inferior in delicacy and reliability to those tests above detailed.]

ALBUMIN DERIVED FROM PUS is present in *relatively small amount*—generally in mere traces, and the urine is hazy when passed.* If *much* pus and *little* albumin be found, then the albumin is probably derived from the pus present. When *much* albumin is present along with pus, suspect renal disease. When *small amounts of albumin occur in urines which are clear when passed* it points more to renal disease (if there are no indications that the condition is functional). *The presence or absence of tube-casts and renal epithelium will also help in forming an opinion as to the source of the albumin in cases of pyuria.*

Before testing urine containing pus for albumin, the pus should be separated by subsidence, or by the centrifuge, and the clear supernatant fluid then tested.†

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* A faint trace of albumin in normal urine may be due merely to nucleo-albumin or to seminal or prostatic fluid.

† The possibility of pyuria being due to leucorrhœa or other vaginal discharge should be borne in mind, and in case of doubt the catheter must be employed.

SIGNIFICANCE AND CAUSATION OF ALBUMINURIA.

Albuminuria { I. *Temporary or Functional.*
II. *Permanent or Organic.*

TEMPORARY ALBUMINURIA.

1. *No tube-casts* (other than hyaline).

2. *Colour, specific gravity and amount passed, normal.*

3. *Amount of albumin generally small.*[*]

4. *Generally the albuminuria is intermittent in character.*

(*a.*) Urine passed on rising may alone contain albumin[†] (if patient remains in bed no albuminuria may occur—orthostatic or postural form).

(*b.*) Albuminuria, again, may only be found after meals especially after breakfast—after prolonged exercise, or cold bathing, and in orthostatic cases may be most marked in the forenoon, and may lessen or even disappear as the day goes on.

So examine samples passed on rising, also about three hours after breakfast, and also one passed after active exercise.

5. Tends to occur mostly in young people, and may disappear altogether on reaching adult life.

6. Absence of symptoms of renal disease.

[*Occasionally the albuminuria of organic renal disease may become intermittent from postural, dietetic, or other causes.*]

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[*] *Nucleo*-albuminuria is apt to be mistaken for true "functional" albuminuria.

[†] It must, however, be remembered that in nearly all *nephritis* cases albumin is to be found in the morning urine.

Some Causes of Temporary Albuminuria.

I. Dyspepsia, functional hepatic disorders, over-eating (too much proteids), physical over-exertion, nervous over-strain (anxiety, examinations, &c.),* general atony, anæmia.

II. Drugs—*e.g.*, turpentine, cantharides, alcohol in large quantities, carbolic acid.

III. Temporary renal congestion in fevers, and occasionally during menstruation (apart from vaginal discharge, or blood, &c., in urine).

ORGANIC ALBUMINURIA.

Altered specific gravity, tube-casts (epithelial, fatty, waxy, blood, &c.), renal epithelium, and as a rule larger amounts of albumin than in the temporary albuminurias are usually to be observed.

(See also Quantitative Albumin estimation, p. 111.)

Some Causes of Organic Albuminuria.

(*a.*) Active and passive renal congestion.

Active as from injury, calculus, &c.

Passive as in pulmonary, cardiac or hepatic disease, abdominal tumours (including pregnancy).

(*b.*) Chronic poisoning—phosphorus, lead, arsenic, iodine, mercury, &c.

(*c.*) Syphilis, Tuberculosis, Gout.

(*d.*) Acute and Chronic Nephritis of all forms, Waxy Kidney, &c.

As regards Life Assurance.—Even when there are no definite signs of renal disease, the general experience is that albuminuric patients as a rule live a shorter time, and that their health tends to become gradually worse. They are always more liable to a break-down in health, and usually display less energy and capacity for work (Grainger Stewart). They are, as a rule, unfit for service in warm climates. As a rule, orthostatic functional albuminurias are entirely recovered from. Where organic kidney disease exists, the life is of course a most risky one, and demands a heavy extra premium.

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* Orthostatic albuminuria has, in adults, been observed in Graves's disease and also in association with movable kidney.

A final decision in doubtful cases should only be made, as a rule, after the patient has been under observation for from nine to twelve months.

DETECTION OF OTHER PROTEIDS IN URINE.

The following are not sought for in the ordinary routine examination, but may be looked for by the following special methods when their presence is suspected:—

SERUM-GLOBULIN.

It is of no practical importance to distinguish between this and serum-albumin.

Although it is known that this may be present by itself in urine, it is nearly always associated with the presence of serum-albumin. Its presence is generally overlooked, as it gives the same reactions as serum-albumin with the various precipitants, *except that on dilution with water the urine gives an opacity with serum globulin, but not with serum-albumin.*

Its importance is said to be due to its prognostic significance in acute Bright's disease as, if sero-globulin is present in large amount in the urine, the prognosis is stated to be more unfavourable. This point is very doubtful, and may practically be disregarded. Globulin alone may occur in hœmaturia, waxy kidney, vesical catarrh, cantharides poisoning, and in certain forms of functional albuminuria. When the urine is strongly alkaline or hyper-acid, globulins are particularly liable to be converted into alkali- or acid-albumin.

The simplest clinical test for globulin is Sir William Roberts's:—

(*a.*) Nearly fill a test tube with water, and then add the urine* drop by drop. Globulin in marked amount is present if each drop leaves a milky streak, and if, on continuing the addition, the water shows a milky opalescence throughout.

(*b.*) Now add a few drops of acetic acid = opalescence disappears.

[The basis of the test is that globulin is insoluble in water, but is redissolved by small quantities of acid. Globulins also dissolve in neutral salt solutions, but separate out on sufficient dilution with water.]

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* The urine must be quite clear. If any opacity, filter till clear.

Crystalline globulin may be *spontaneously* thrown down as a white ppt. from the urine on standing. When this ppt. is shaken up it gives a watered-silk appearance throughout the urine. Microscopically the ppt. is seen to consist of long rhomboidal crystals with the angles cut away. These may be aggregated as stars or rosettes. Such a deposit occurs very rarely.

ALBUMOSES OR PROTEOSES are derived from the hydration of proteids, and normally occur as intermediate products of peptic and pancreatic activity, being then further hydrated into peptones before absorption from the gastro-intestinal tract. From each kind of proteid a proto-, hetero- and deutero-proteose (albumose) can be obtained.

The proto- and hetero-varieties are termed *primary* albumoses. The deutero-varieties are termed *secondary* albumoses.

Proto-albumoses so far have not been detected in urine (Sidney Martin).* Deutero- and hetero-albumoses are found generally alone but also in conjunction with sero-albumin and sero-globulin (especially in nephritis). *It is at present a matter of no clinical importance to distinguish between the different varieties of albumose.*

Deutero-albumose and peptone are generally but incorrectly classed as peptonuria. There is much room for doubt as to whether *true peptones* are ever detected in urine. Nearly all the observations which have been published as to the detection of peptonuria were made before the albumoses had been as much worked at as they have now been. There seems to be considerable likelihood that what were described as peptones, were mostly *deutero-*

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* This point is still doubtful, as, on the other hand, Dr. Lockhart Gillespie states that he has found proto-albumoses in urine. Further confirmation is required.

albumoses.[*] It would be better to term the occurrence of hetero- and deutero-albumoses, *albumosuria*; and of pure peptones, *peptonuria.*

Albumoses in the urine have been found in connection with Empyema, phthisis, resolving pneumonia, infectious fevers, nephritis (probably suppurative, and also in "granular contracted kidney"), ulcer or cancer of stomach or intestine, and chronic abscesses, and especially in diffuse myeloid sarcoma and osteomalacia.

Albumosuria not infrequently occurs during the normal puerperium.[†] According to v. Jaksch, albumosuria occurs in epidemic cerebro-spinal meningitis but not in tubercular meningitis, but this requires further confirmation. In certain acute inflammations the onset of suppuration has been accompanied by albumosuria, but it is still uncertain whether this is a constant sign or not. It may be formed by partial digestion of proteids in the bladder by ferments.

The clinical significance (prognostic or diagnostic) of albumosuria is, therefore, at present uncertain further than that its occurrence is usually pathological.

DETECTION OF ALBUMOSES IN URINE.

The behaviour of *hetero*-albumose with the heat and HNO_3 tests, and of *deutero*-albumose with picric acid in applying the albumin tests, as herein advised, will generally serve to indicate the presence of these substances. An additional simple confirmatory test is the following, which will cause the pptn. of albumins as well as of albumoses (and peptones), the latter two being distinguished by dissolving on heating:—

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[*] [The so-called "Bence-Jones's albumose" is hetero-albumose.]

[†] Through the courtesy of Professor A. R. Simpson and the Resident Medical Officers of the Edinburgh Maternity Hospital, I have had the opportunity of examining a number of urine samples (drawn off by catheter), from puerperal women. Traces of albumoses (chiefly deutero), were detected in several normal cases, but in the vast majority albumosuria was absent. In one case of puerperal eclampsia in which the urine was highly albuminous, traces of both hetero- and deutero-albumoses were present.

Salicyl-sulphonic acid test:—

1. To about a two inch depth of filtered urine in a test-tube add two drops of a saturated solution of pure salicyl-sulphonic acid (or a few crystals of this reagent) = white ppt. or turbidity if any urinary proteid is present.

2. Heat = ppt. dissolves, but reappears on cooling = *albumoses* (or peptone).

3. Boil = ppt. does not dissolve, but becomes coagulated in lumps = *serum-albumin or globulin.*

Ppt. diminishes, but does not disappear = *albumin and albumose.*

Note.—Salicyl-sulphonic acid when pure does not deteriorate on keeping. If impure, its solution reddens when kept for some time.

[The *quantitative estimation of albumoses* (and of peptones) in urine is at present of no clinical importance. The methods, in any case, are rather too elaborate for clinical employment.]

PEPTONES.* — As stated previously, there is much likelihood that what has hitherto been described as peptonuria was in reality deutero-albumosuria.

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* The presence of peptones in the urine in traces has been alleged to be physiological, and to be occasionally due to absorption of unchanged alimentary peptones, or to the transformation of proteid inflammatory products. This condition (*deutero-albumosuria* rather than *peptonuria*) has been described as present in many suppurative conditions—*e.g.*, purulent effusions into serous cavities, phthisis; also in most fevers—*e.g.*, Malaria, diphtheria, typhus, scarlatina, erysipelas, variola, cerebro-spinal meningitis, septicœmia, typhoid, and in carcinoma, acute nephritis, catarrhal jaundice, scurvy, purpura hæmorrhagica, croupous pneumonia (during resolution stage), apoplexy, tertiary syphilis, phosphorus poisoning, in pregnancy and the puerperium, and in uterine myomata or para- or perimetritis.

It may be mentioned that while the author has frequently encountered albumoses in urines, a search for true peptones has always proved negative. On the supposition, however, that true peptones *may* occur in urine, the following process for their detection is given :—

Method for detecting Peptones :—

1. By boiling and HNO_3 tests = no result (if albumin is present, first coagulate it by boiling, and filter it off).

2. Add powdered ammonium sulphate to the filtered urine, and shake up till no more dissolves = no ppt. with peptones; = if a ppt. (albumoses), filter it off, and test the *filtrate* for peptones.

3. With picric acid test = ppt. or opacity, *soluble on heating = peptones.*

Confirm by the *Biuret test* *:—

(*a*.) Add a drop or two of 1 per cent. cupric sulphate solution to the filtrate concentrated to a thick syrupy consistence.

(*b*.) Then add a *considerable excess* of liquor potassæ = rose-pink colour due to peptones.

WHEN TWO OR MORE PROTEIDS OCCUR AT THE SAME TIME :—

(1.) Treat some of the urine with salicyl-sulphonic acid = white ppt. (albumins, albumoses, peptone).

(2.) Boil the solution = permanent coagulum = ALBUMINS;
= ppt. dissolves = ALBUMOSES ;
= ppt. markedly lessens, but does not clear up = ALBUMINS AND ALBUMOSES.

(3.) Filter *while hot* = ppt. *forms on cooling* = ALBUMOSES.

(4.) Again filter off albumose ppt., and apply the

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* This gives a rose-pink colour with peptones and albumoses, but *as albumoses (and all other proteids, except peptones), have been pptd. by the ammonium sulphate* and filtered off, a rose-pink colour will be caused only by peptone.

Biuret test to the concentrated filtrate = a rose-pink colour = PEPTONES.

Or instead apply the Picric Acid test = ppt., soluble on heating.

Alternative Method for the Detection of Albumoses and Peptones in Urine.

The following alternative process is based on the facts that:—

1. Proto- and hetero-albumoses are pptd. by saturation of the solution with sodium chloride or ammonium sulphate. Deutero-albumose is not pptd. by sodium chloride, and can thus be separated from them.

2. Peptones are not pptd. by ammonium sulphate, and can thus be separated from all albumoses and other urinary proteids.

3. Cold strong HNO_3 ppts. proto- and hetero-albumoses: but *proto- is hardly at all soluble on heating, while hetero- readily dissolves on heating.** Deutero-albumoses are not pptd. by HNO_3 *unless the solution has been previously saturated with sodium chloride.*

Detection of primary and secondary albumoses:—

1. Get rid of any albumin present by boiling the acid urine and filtering off the albumin-coagulum.

2. Evaporate filtrate to a small bulk.

3. Then add common salt, and shake up till no more dissolves = *primary albumoses* (proto- or hetero-) *will be pptd.*

4. Filter and to the filtrate add cold strong nitric acid, drop by drop, so long as an opacity results = secondary (deutero-) albumoses will be pptd.

5. Heat ppt. = *disappears, but returns on cooling.*

Hetero-albumose:—

1. Heat the upper layer of some of the acid urine placed in a test-tube. Opacity = phosphates, hetero-albumose or albumin.

2. Boil. Opacity clears up = hetero-albumose. Add a drop of strong HNO_3, and opacity clears up = phosphates. Opacity does not clear up = albumin.

Confirm—Add, drop by drop, cold strong HNO_3 = opacity or ppt., *soluble on heating, but returning on cooling* = hetero-albumose.

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* Proto- and hetero-albumoses in solution can be distinguished by adding to the concentrated solution an equal bulk of methylated spirit = hetero-albumose is pptd.: proto-albumose is *not* pptd.

Deutero-albumose:—

1. First ascertain presence or absence of hetero-albumose, as above.

2. Remove any albumin by boiling and filtration.

3. Next concentrate the filtrate by evaporation to a quarter of its bulk.

4. Now remove peptones by saturating the urine with ammonium sulphate = ppt. of hetero-albumose (peptones are *not* pptd.).

5. Filter off this ppt., and apply to it the Biuret test = *rose-pink colour* if deutero-albumose is present.

Confirm by adding common salt to a portion of the concentrated urine (to which ammonium-sulphate has not been added) *until saturated.* Then add HNO_3, drop by drop = ppt. soluble on heating, but reappearing on cooling = deutero-albumose.

Peptones.—To the concentrated *filtrate*, obtained after adding ammonium sulphate in testing for deutero-albumose, apply the Biuret reaction = rose-pink colour = peptones.

MUCIN is the chief constituent of mucus. When *much* mucin is present in the urine it usually points to a catarrhal condition of the urinary tract. Mucin is slightly soluble in neutral or alkaline urines, and is pptd. from acid urines. Heating does not ppt. it. Mucin is *detected* by diluting the urine with an equal bulk of water, and then adding *excess* of acetic acid = ppt. of mucin, *soluble with difficulty in excess of the acid,** and increased by boiling. The chief clinical interest of mucin is the fact that it is occasionally mistaken for albumin.

Mucin will be distinguished from albumin in urine if (1.) The rule given previously be followed *as to always filtering the urine previous to testing for albumin*, for in this way most of the mucus is got rid of.

(2.) With the HNO_3 test, by observing that a mucin cloud forms towards the *upper* surface of the urine and not at the junction of the fluids as with albumin.

(3.) Also *if the direction be followed as to always*

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* A ppt. of *Nucleo-albumin* produced by acetic acid is *moderately soluble* in excess of the acid.

employing the heat and picric acid tests for albumin, in addition to the nitric acid test, for mucin is not pptd. by picric acid or by boiling, while albumin is. *No other acid —e.g., acetic, should have been added to the urine before applying the latter tests, otherwise there may be a precipitate with mucin.*

Pus is distinguished from mucin by forming a gelatinous mass on addition of liquor potassæ. Mucin dissolves on adding liquor potassæ.

NUCLEO-ALBUMIN, which in urine is largely derived from the epithelium of the urinary tract, closely resembles mucin in physical properties: by its solubility on adding an alkali, and in being pptd. by acetic acid, or HNO_3, *but not by the heat test.* It is of little clinical importance except as interfering with the albumin tests. It is often present in large amount in leucocythæmia, and in inflammations of any part of the urinary tract.

If any further doubt were to occur as to either mucin or nucleo-albumin interfering with the albumin tests*:—

Compare the result obtained with HNO_3, with and without previous dilution of the urine with an equal bulk of water. With the diluted urine = more pronounced reaction (mucin or nucleo-albumin).†

BLOOD.—*Hæmaturia* is the condition in which all the constituents of blood appear in the urine.

In *hæmoglobinuria* no blood corpuscles may be present in the urine but hæmoglobin is present.

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* *Mucin and nucleo-albumin* can only be *distinguished accurately from each other in mixture* when present in large amount, and by detecting the presence of phosphorus which exists in nucleo-albumin but not in mucin. This may be done by boiling one portion of the ppt. (given with strong acetic acid) with dilute HCl, neutralising and then applying Fehling's test (see p. 84) for *mucin.* The other portion of the ppt. is fused, the ash dissolved in HNO_3, and if a yellow ppt. is obtained (on heating) with ammonium-molybdate solution, *nucleo-albumin* is present. This is too complicated a process for clinical use, but is given to show the method of distinguishing between these two substances.

† These two substances, according to Purdy, can be eliminated for all practical testing purposes by merely *saturating the urine with common salt before adding acetic acid and heating.*

(1.) *In examining a sample for blood always endeavour to examine it as soon as possible after being passed, for in very dilute or in alkaline urines the corpuscles tend to swell up and disappear.*

(2.) When enough blood is present to cause a reddish-brown ("smoky") appearance, only *traces* of albumin may be detected in the urine.*

(3.) If the urine is *acid* and much blood is present the colour will generally be *dark red.*

(4.) If the urine be *alkaline*, it will generally be *bright red.*

(5.) In *concentrated urine* the presence of small amounts of blood may not be in any way indicated by the colour.

(6.) *Blood from the bladder or urethra*† gives generally a *bright-red colour* to the urine and *clots may also be present.* If *from the kidneys*, the colour may be *duller* and the urine will be *hazy;* and may throw down a reddish deposit or one like coffee grounds.

(7.) Albumin is present—often thick brownish flakes float on surface after boiling a urine containing blood.

(8.) The microscopic appearance of the deposit readily shows the presence of hæmaturia.

Hæmoglobinuria, or the presence of blood-pigment in hæmaturia, may be detected by—

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* One part of blood in 1500 parts of urine gives a smoky tint while 1 in 500 gives a bright cherry colour (Ralfe).

† Blood from the kidney is generally intimately mixed with the urine.

Blood from the bladder occurs especially at end of micturition.

Blood from the urethra frequently escapes between acts of micturition.

Urethroscopy or cystoscopy is, of course, a valuable aid in localising the source of hæmorrhage.

I. GUAIAC TEST:—

(*a.*) If the urine be neutral or alkaline, acidify it.

(*b.*) Then pour some tincture of guaiac* into a test-tube and add about an equal bulk of ozonic ether or of turpentine which has been ozonised by leaving it exposed to the light for some time. Note any trace of blue colour. If absent, the reagents are satisfactory.

(*c.*) Then pour some urine gently on the surface of the guaiac and ozonised ether or turpentine solution, inclining the test-tube to do so. A blue zone forms at once *at the plane of contact* = blood.

If the blue colour is diffused through the urine = an iodide may be present.

(*d.*) Now heat and *if the blue colour goes* the colour is due to pus.†

The test can also be conducted by moistening a piece of white blotting-paper with a few drops of the urine. Then allow to dry. Then let fall a drop of tincture of guaiac on the stained portion, followed by a few drops of the ozonised ether or turpentine = blue colour.

If no reaction is given with this test it may safely be concluded that blood pigment is absent. A positive reaction, however, does not certainly indicate its presence.‡ For Iodides, Sputum or nasal mucus give a similar reaction and a distinction can only be made in this case by means of the Spectroscope which will give the blood spectrum.*

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* Keep the guaiac solution in a blue or brown glass bottle as, otherwise, it deteriorates. *The Guaiac Tincture must be made with rectified spirit. The Ammoniated Tincture of Guaiac must not be used.*

† Ozonic ether when added to urine containing a marked amount of pus often causes effervescence.

‡ The Guaiac test is an exceedingly delicate one. It is believed that the hæmoglobin carries oxygen from the ozonised turpentine or ether to the guaiac which is oxidised to a blue compound.

ALTERNATIVE TESTS FOR BLOOD PIGMENT :—

Neither of the succeeding tests are of as much value as the Guaiac test.

II. HELLER'S TEST :—

(*a.*) Heat the faintly acid urine to boiling = mottled ppt. of albumin and hæmatin.

(*b.*) While boiling add some liq. potassæ = ppt. dissolves and then a brownish-red ppt. re-forms (earthy phosphates and hæmatin), and if some drops of the supernatant fluid be placed between two microscope slides and held up to the light the colour is green.

Caution.—Rhubarb, senna, and santonin, when being excreted in the urine, give the same reaction. Furthermore, if the urine was alkaline originally, no ppt. may occur until a few drops of lime-water solution have been added.

III. THE HÆMIN TEST :—

(*a.*) Evaporate some of the sediment to dryness along with a crystal or two of common salt.

(*b.*) Then add a drop or two of glacial acetic acid to the residue ; and

(*c.*) Place on a microscope slide and *heat gently.*

(*d.*) Cool and examine under the microscope = reddish-brown rhomboidal crystals of hæmin.

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* See Appendix C.

HÆMATURIA may be present in Acute Nephritis (especially the parenchymatous form,—post-scarlatinal or malarial); calculi of the renal pelvis, new growths; scurvy, purpura; eruptive fevers, embolism (*e.g.*, endocarditis and in "surgical kidney"); severe blow on or strain of lumbar region; certain parasites; cantharides or turpentine poisoning; "back-pressure" in cardiac disease; tuberculosis of kidney; cystic disease (*e.g.*, sudden copious hæmorrhage from a burst cyst).

METHÆMOGLOBIN is formed in acid urine which contains blood especially when the source is the kidneys or when the urine has stood for some time. It can only be identified by the spectroscope.

HÆMOGLOBINURIA has been described in Pyœmia, Smallpox, Malaria[*] and in the "Paroxysmal" condition, Typhus, after extensive burns, Purpura, Scurvy; after transfusion of blood; Insolation; Syphilis; Mushroom poisoning; Raynaud's disease; when Quinine, Carbolic acid, Pyrogallol, Potassium Chlorate, Phosphorus, Arseniuretted Hydrogen, Hydrochloric or Sulphuric acids are being taken into the system in poisonous quantity. The hæmoglobin occurs as oxyhæmoglobin mixed with Methæmoglobin in excess.

HÆMATOPORPHYRIN.[†] When hæmatin devoid of iron is present in the urine it causes, when in large amount, a dark purplish-red colour. The Guaiac test fails to give a definite reaction, and here again the spectroscope alone leads to the identification of the substance.[‡] This condition occurs when sulphonal is being taken in dangerous amount, but has been occasionally noted in cases of Addison's disease, *intestinal hæmorrhage*, cancer, typhoid fever, plumbism, and hepatic cirrhosis.

FIBRINURIA. The urine is reddish-yellow when passed, but rapidly flakes or reddish or reddish-yellow clots appear in it, and it becomes of jelly-like consistence—throughout if very much fibrin be present, or at the foot of the vessel if the quantity be small.

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[*] Renal casts and renal epithelium are—at least in the early stages—absent, but in one type of tropical hæmoglobinuria a parenchymatous nephritis supervenes not infrequently, in which case casts and renal epithelium will be found.

[†] It may occur in normal urine in very small quantity.

[‡] See Appendix C.

The microscope shows that these coagula consist of a network of fine threads of delicate structure. Blood corpuscles, fat cells, &c., are often entangled in this network. This appearance is distinctive. If the supply of light is lessened (as when for the microscope mirror a piece of polished brass is substituted), this fibrillary structure is shown up very well as delicate, white interlacing threads against a dark back-ground.

It is a rare condition found principally in cases of chyluria, hæmaturia, of violent inflammations of the kidneys or urinary passages, of bladder-tumour or tuberculosis of the bladder and in cantharides poisoning.

FURTHER MEANS FOR DETECTION OF FIBRIN :—

Filter off the fibrin and treat it with

(*a.*) Hydrochloric acid = it swells up but does not dissolve.
Add some pepsin now = the fibrin dissolves.

(*b.*) It is insoluble in water.

(*c.*) Treat with a 1 per cent. solution of Sodium Carbonate and heat gently for some time. Filter and add Millon's reagent* to the filtrate = dark red colour.

FIBRIN IS DISTINGUISHED FROM PUS THUS :—

(*a.*) Pus thins on adding water : Fibrin does not.

(*b.*) Treated with Liq. Potasse, Pus swells up and becomes gelatinous. Fibrin does not.

CHYLURIA.—(*a.*) The urine is thick and yellowish-white (milky) from suspended small fat globules. The fat may form an oily layer or creamy flakes on the surface *on standing.*

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* Millon's reagent : mix one part of mercury and two parts of strong nitric acid and heat till dissolved. Then add twice its volume of water and allow to settle and filter. The *filtrate* is Millon's reagent.

(*b.*) If the urine be shaken up with ether, the fat is dissolved, and the urine may become of normal appearance, especially if an alkali be added to it. (The urine can now be examined as ordinarily.)

(*c.*) A faint pink tint from blood is also often present, and the blood separates later as a pinkish-red ppt., which becomes much pinker on longer exposure (fibrinuria, *which see*).

(*d.*) Coagulation occurs on standing, and whitish clots of fibrin separate out, and may float on the surface as a pink or creamy gelatinous layer, with underlying turbid urine. Often the more fibrin present the less fat is found.

(*e.*) Examine under microscope = an enormous quantity of fine fat-globules, and also many leucocytes, erythrocytes, and epithelial cells. Filariæ may be found, particularly in the night-urine, and often moving actively.

(*f.*) The urine's specific gravity is somewhat lower than normal, and as the *urea and chlorides* are generally found to be *lessened* in amount, this is readily explained. The *phosphates* may be notably *increased*. Albuminuria is present and, occasionally, albumosuria.

(*g.*) Chylous urine may only be passed during the night or in the morning. It may frequently happen that the morning urine is the only chylous specimen passed during the twenty-four hours.

Urine passed during the night by a chyluric patient is usually markedly chylous.

LIPURIA, OR FAT IN THE URINE.

Besides occurring in chyluria, fat occasionally is found in small quantities in "large white kidney," generally in association with fatty casts and fatty epithelium, and also in diabetes mellitus, acute phosphorus poisoning, cystitis, fat embolism in fracture involving the bone-marrow particularly, and in certain pancreatic diseases. Fat may also occur as needle-like crystals occasionally in the form of sheaves, stars, and irregularly grouped bundles. Such arc occasionally derived from vulvar or preputial smegma. Fat globules are best stained by an *alcoholic* solution of a disazo-stain, termed "Sudan III." The solution has a brownish-red colour, and stains only fat an *orange-red colour*. Osmic acid is unreliable, as it stains other substances besides fat.

SUGAR.

GLYCOSURIA.—Glucose is normally present in such small amounts as to escape detection by the ordinary tests (except perhaps that with phenyl-hydrazine), but is readily distinguished by appropriate tests when present in pathological amount. By the term "diabetic urine" is meant the renal secretion of persons suffering from diabetes mellitus, for the polyuria associated with d. insipidus is not accompanied by the presence of glucose in the urine.

Temporary glycosuria is met with in a large number of diseases, and also may result from the action of various drugs. It has been reported as occurring in gouty people; after an epileptic, asthmatic, whooping-cough, or hysterical seizure; after an attack of ague; sciatica; recovery from cholera; worry, overstrain, or severe trauma to brain or spinal cord; occasionally after administration of ether, chloroform, chloral, salol, antipyrin; carbonic oxide poisoning, and particularly by phloridzin which produces a true glycosuria when administered. But it must be noted that when produced by chemical agents this condition is very often apparent and not real, as many drugs cause the elimination by the urine of reducing agents—*e.g.*, glycuronic acid, which give reactions resembling those given by glucose. A mild *temporary* glycosuria may follow gastric disorder, or the excessive use of sugary and starchy foods, and in such cases it ceases when the gastric condition is remedied, or on diminishing the amount of carbohydrates in the diet.

In temporary glycosuria the appearance and daily amount of the urine is *usually* unaltered (but this also occurs occasionally in diabetes mellitus).

Persistent glycosuria points to hepatic, pancreatic, or cerebral disease of a grave nature—especially in persons under twenty years of age. In those over fifty the course of the disease is generally milder and more tractable.

In cases of carbuncle, boils, cataract, or pruritus, examine the urine for sugar specially, as these conditions may be incidents in the course of a hitherto undetected case of diabetes mellitus.

DIABETIC URINE GENERALLY SHOWS THE FOLLOWING CHARACTERS:—

(1.) *Very marked increase in the daily amount* of urine, the appearance is *brighter* than usual, and there is also *great pallor* from dilution of the urinary pigments. Occasionally a pale greenish tint prevails. But *polyuria may be absent*, and *the urine may be of a dark colour*, especially in mild cases. As a rule, when less than 100 ozs. daily are being passed, the physical characters are not markedly changed. In ordinary polyuric cases from 8 to 15 pints of urine a day are voided, but as much as 20 pints a day have been passed.

(2.) Apple-like, whey-like, or hay-like odour; or later, alcoholic or somewhat chloroform-like.*

(3.) Froths easily, and froth remains a long time.

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* This odour is now believed to be due more to aceto-acetic acid than to acetone.

(4.) Generally *markedly acid reaction* (even after meals or during administration of alkaline medicines).

(5.) Usually a high specific gravity (1030–60) but very often the specific gravity is very much lowered, and I have even seen 1004 in an otherwise typical case.

(6.) The *total amount* of urea is *generally* increased (due to increased tissue-waste and, to a certain extent, to the largely proteid diet prescribed) but on account of dilution the *percentage* is usually diminished.

(7.) Albuminuria is not generally present till late on in the disease. Tube-casts are rare.

(8.) The proportion of sugar may vary considerably, 1–3 or 4 per cent. in an ordinary case, but 8 to (it is stated) 15 in much severer cases. From ½ oz. to 2 lbs. of glucose may be lost daily. It is found in largest amount three or four hours after meals and least in the morning urine.*

The amount varies directly as the amount of carbohydrates in the diet and, prognostically, a large amount is of grave significance when the patient is on a strict "diabetic" diet, when, as a rule, in favourable cases it falls to 1 per cent. or less.

DETECTION OF SUGAR.

Before testing for sugar, albumin must be removed by boiling and filtering the acid urine.

In testing for glucose in urine the author's routine practice is to apply either the Safranine or Fehling's test and to confirm, if any doubt arise, by means of the phenyl-hydrazine test.

Negative results with any of these tests excludes the presence in pathological amount of glucose.

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* Insects are specially attracted to diabetic urine.

I. SAFRANINE TEST.

Safranine is a coal-tar dye—a brownish-red powder—and forms with water a blood-red solution. When boiled in the presence of glucose and caustic potash the safranine is reduced to its corresponding leuco-derivative which is pptd.

(1.) *Take equal parts of*—
  (*a*) the *albumin-free* urine;
  (*b*) of liquor potassæ (B.P.);*
  (*c*) and of 1–1000 solution of safranine (*i.e.*, ·35 gramme, or about 5 grains of safranine dissolved in 33 c.c. of distilled water). The resulting mixture is dark blood-red and opaque.

(2.) Boil this mixture in a test-tube but *avoid* as much as possible *shaking up* the mixture. Then cool—if more than $\frac{1}{10}$th per cent. of glucose be present the opaque RED colour disappears,—a YELLOW colour taking its place.

When there is only a *small amount* of glucose present the red colour *partially reappears when the solution is shaken up.* The *surface* of the fluid in the test-tube is always somewhat red from contact with air but this (as well as any small red floating flakes) is to be neglected when the rest of the fluid remains no longer an opaque red but becomes *brownish yellow—opaque when much glucose* is present *but clear when only traces are present.*

This test is the simplest and fortunately also one of the surest tests for glucose and is not interfered with by the presence of uric acid, hippuric acid, creatinin, nor apparently by glycuronic acid.* The solutions required keep well and are much more readily prepared than Fehling's or other reagent.

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* Care must be taken that the liquor potassæ is free from lead and it must not be too old. Small quantities should be obtained at one time so that the solution may be frequently renewed.

If a *marked* reaction is obtained with this test it is usually needless to apply another confirmatory test.

II. PHENYL-HYDRAZINE TEST.

(1.) To a two-inch column of *albumin-free* urine in a test-tube add as much phenyl-hydrazine hydrochloride (crystalline) as will lie on the point of a pen-knife (say about 8 grains or about 0·5 grm.).

(2.) Then add about twice as much powdered sodium acetate.

(3.) Place the test-tube in a beaker or other vessel containing boiling water and boil for 30 minutes.

(4.) Then allow to cool = crystalline or amorphous yellowish ppt. (brick-red occasionally), if glucose is present.

If the ppt. is AMORPHOUS :—

(*a.*) Dissolve it in *hot alcohol.*

(*b.*) Dilute with water.

(*c.*) Boil off the alcohol = yellow crystals of glucosazone are pptd.

(5.) Examine the crystals under the microscope = *yellow or brownish yellow needle-like crystals arranged in fans, stars, or sheaves.*

It is particularly necessary to examine the ppt. microscopically when only traces of glucose are present

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* I find that the otherwise normal urine of patients taking chloral or chloroform gives no reaction with safranine and that these drugs when placed in normal urine reduce Fehling's solution but do not give the safranine reaction.

—*i.e.*, where only a turbidity or very faint ppt. has resulted.[*]

NEUMANN'S METHOD is an excellent alternative way of conducting the test.

(1.) To 5 c.c. of albumin-free urine add 2 c.c. of Acetic Acid (50 % strength *and saturated with Sodium Acetate*) and 2 drops of pure phenyl-hydrazine.[†]

(2.) Evaporate to half its bulk.

(3.) Cool under the tap.

(4.) Warm slightly.

(5.) Then allow to cool gradually = yellow crystals separate out, if glucose is present.

The Phenyl-Hydrazine test does not depend on any reducing action—a great advantage—and hence urea, uric acid, xanthin, creatinin, &c., do not interfere with the test.

It is also of all sugar tests the most delicate. It shows ·005 per cent. ($\frac{1}{40}$ grain per oz.) of glucose. The test is so delicate that it may show even the faint traces of glucose present in normal urine. So if a *slight* reaction be obtained with this test, and no reaction occurs with the Safranine or Fehling's solution, it may be concluded that the quantity of sugar present is *not* pathological, and may therefore be disregarded.

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[*] *Riegler's Modification* of the test is as follows :—

(*a.*) Put 2 grains of phenyl-hydrazine hydrochloride crystals in a capsule along with 7 grains of sodium acetate.

(*b.*) Add 20 drops of urine (albumin-free) and *boil.*

(*c.*) Then remove from the flame and add 25 drops of caustic potash or soda (10 per cent. strength) = *red violet colour* appears within a minute if glucose is present in pathological amount.

[†] (*a.*) *Not the hydrochloride.*

(*b.*) Neumann employs a special bulbed test-tube, graduated at 3, 5 and 7 c.cs. This enables the evaporation to be conducted more rapidly, as the tube while being boiled can be held in an almost horizontal position.

CAUTIONS AS REGARDS THE PHENYL-HYDRAZINE TEST.

1. *Levulose* (which occasionally occurs along with glucose in urine) yields an osazone, indistinguishable from glucosazone. The polarimeter best distinguishes one from the other, as levulose reacts like glucose with the reduction and fermentation tests.

2. *Lactose* is occasionally to be found in the urine of nursing women and also may occur towards the end of pregnancy. It reacts *much less readily* to the above test, but gives similarly coloured crystals, which (like Maltose) *do not separate out till after cooling.* Under the microscope phenyl-lactosazone forms generally somewhat denser stars than phenyl-glucosazone and also forms wide prisms. *The fermentation test* gives a negative result with lactose.* The history of the case or the following colour-test will readily clear up the point †:—

(*a.*) Filter off the crystals and dry.

(*b.*) Add a drop of strong sulphuric acid.

(*c.*) Then add a crystal of black oxide (dioxide) of manganese = *purple colour* shows phenyl-glucosazone and therefore glucose. ‡

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* See also p. 87.

† The determination of the melting point of the crystals and the different degrees of solubility are the most accurate methods of distinguishing the various osazone crystals.

These are, however, impracticable methods for clinical application.

‡ Strychnia reacts similarly, except that the purple colour changes later to cherry-red.

3. *Glycuronic Acid or Glycuronates.*—The occurrence of these substances is to be specially remembered in conducting this test. These substances are occasional precursors of glucose in diabetes. They are pptd. as a brown resinous mass which under the microscope is *amorphous* or forms yellow *scales* (not needles). And if the heating is conducted for a sufficient time there is less risk of the deposit of the yellow *crystals* of glycuronic acid which will then tend to assume the brown, resinous, amorphous form.

4. Do not let the phenyl-hydrazine touch the fingers as it may produce severe irritation.

5. *Maltose* has been described as occurring in diabetic urine. It forms yellowish phenyl-maltosazone needle-shaped crystals, but these are distinguished from those produced by glucose and lactose by being much broader than either and by their different grouping (see figure), and they do not form wide prisms like lactose.

6. The pentoses (see p. 91) may react with phenyl-hydrazine producing citron-yellow crystals (phenyl-pentosazone). Any difficulty on this point can best be settled by testing the urine afresh by the *fermentation* test, which gives a negative reaction with pentoses and a positive with glucose.

III. FEHLING'S TEST.

This is perhaps the most popular test of all, but is much inferior in both delicacy and accuracy to both the preceding and rather more troublesome to apply than the Safranine test. Tests such as Fehling's (which depend on the reduction by glucose of cupric salts, in hot alkaline solution, to the condition of the brick-red or yellow cuprous oxide) may mislead owing to the co-existence of uric acid, excess of urates or of creatinin, alcapton, hippuric acid, and *above all of glycuronic acid.* This reduction of the cupric salt by uric acid, glycuronic acid, &c., is specially apt to occur if the solution is boiled,* or if the urine is too concentrated.†

THEREFORE, TO FREE THE URINE FROM THESE REDUCING AGENTS—*i.e., where a doubtful reaction has been obtained* to make certain that the result is really produced by glucose,—it is necessary to add to the urine *while boiling* about a quarter of its bulk of hot lead acetate solution (10 per cent. strength).

The urine is then filtered and the filtrate tested. (The lead solution ppts. uric acid, albumin, phosphates, sulphates, and pigments, but not sugar.)

IF THE URINE IS AMMONIACAL, FEHLING'S TEST IS USELESS.

Fehling's solution is prepared thus:—

(*a.*) Dissolve 34·64 grammes of pure cupric sulphate in hot distilled water, and when cool add distilled water to make up the bulk to 500 c.c.

(*b.*) Dissolve 173 grammes of Potassium Sodium Tartrate (Rochelle salt) in 300 c.c. of hot water, and add 60 grammes of stick caustic soda. Cool and make up with water to 500 c.c.

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* Glycuronic acid may occur normally in very minute quantities in urine.

† In *normal* urine the quantity of these reducing substances is usually too small to cause reduction and, if the test be conducted as described herein, no difficulty should be experienced on this score.

Keep these solutions (a) *and* (b) *separate* as they spoil when kept mixed and give wrong results:[*] hence *do not mix until about to perform a test for sugar.* Then mix them in equal volumes (until quite clear), and then proceed with the test as follows:—

(1.) Boil about 1 inch depth of Fehling's solution in a test-tube to see that it has not become spoilt by keeping. If it becomes turbid or loses its blue colour, it is unfit for use.

(2.) Then add to the hot Fehling's solution *three or four drops* of the albumin-free urine,[†] and again heat, *but not to boiling point.* If much glucose be present, a brick red or yellow ppt.[‡] of cuprous oxide results.

(3.) If no result, add gradually and drop by drop more urine—continuing the heating—until by degrees *an equal bulk* of urine has been added. Bring almost to boiling point and cool. If then no result = urine contains less than $\frac{1}{5}$th °/₀ of glucose. When less than a $\frac{1}{2}$ °/₀ of glucose is present *the ppt. does not occur until the urine cools* — the urine becoming first an *opaque greenish colour.*

Uric acid, glycuronic acid, creatinin and other reducing agents generally give less marked reactions than glucose—e.g., a greenish-brown colour, coming, as a rule, slowly.

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[*] Racemic acid is probably produced from the tartrate and reduces cupric oxide.

[†] Phosphates, *if abundant,* may be removed by adding Sodium Carbonate solution, boiling and filtering. Ordinarily this is unnecessary.

[‡] Brick-red ppt. = anhydrous cuprous oxide;
Yellow ppt. = hydrated cuprous oxide.

This is specially apt to occur on prolonged boiling, which may further cause *ammonia* to be formed (from the interaction of alkali and nitrogenous substances), and this may keep the cuprous oxide in solution. Cuprous oxide may also be dissolved when excess of glucose is present, hence the direction to add only a few drops of urine at a time to the Fehling's solution.

If more glucose is present than is required to reduce the cupric oxide, then the former is apt to become *caramelised*, and particularly on prolonged boiling. The ppt. and superjacent urine in such a case become of a dark brownish colour.

Note.—Glucose reduces the cupric oxide below the boiling point. Most of the other reducing substances in urine require to be heated to boiling before they can reduce the cupric oxide.

[The administration of Saccharin, so often given to diabetics, has no reducing effect on Fehling's solution.]

FERMENTATION TEST depends on the decomposition of glucose by yeast into carbon dioxide gas, alcohol, glycerine, succinic acid, &c.

Advantages—This test is the best for clinical purposes for distinguishing glucose from other substances* which may be mistaken for it—viz., glycuronic acid, pentoses, cane sugar, lactose,† &c. Cane sugar and lactose will ultimately ferment (after "inversion"), but this will not have set in until *after* about 24 hours have elapsed. They are thus readily distinguished from glucose, which usually has shown marked signs of fermentation within from 12 to 18 hours.

Disadvantages—

(1.) It takes a relatively long time to carry out, 12 to 18 hours.

(2.) It is often difficult to obtain fresh yeast, and even when procured the yeast is uncertain in its action as sometimes it proves inactive, and besides it has to be proved that it contains no starch which would itself give the reaction.

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* *Levulose* has also been known to occur in urine. It gives most of the glucose reactions, ferments with yeast, yields an osazone similar to glucosazone, and can only be distinguished by polarimetry.

† Inosite, the so-called "muscle-sugar," is not a sugar, but a member of the aromatic series. It may occur along with glucose in diabetes. It differs in its reactions from the sugars completely.

(3.) It is unreliable with less than a ½ per cent. of glucose in any case.*

METHOD :—1. First see that the yeast is free from starch by pouring a few drops of B.P. Tincture of Iodine on one or two portions of it = blue colour if starch is present. *Well-washed* fresh brewer's yeast is preferable, as pressed yeast very frequently contains much more starch.

2. Then boil some of the urine in a capsule or beaker for about ten minutes in order to expel the air from it. *Cool.* Then unless the urine is markedly acid, render it so by means of acetic acid (for alkaline urine is fermentable even in the absence of sugar).

3. Then place a piece of yeast about the size of a pea in the urine and dissolve the yeast in it completely by stirring.

4. Then completely fill the graduated limb of a Doremus's ureometer (see p. 122) with the urine. Take care that no air is left at the top of the tube. (A test-tube inverted in a beaker containing quicksilver may be used instead of the Doremus apparatus.)

5. Allow to stand 12 to 18 hours in a warm place—*e.g.*, mantelpiece,† and then see if any gas has formed at the top of the tube.

6. *The following control experiments ought to be performed side by side with this* :—

Repeat the experiment exactly as above, but using :—

(*a.*) Distilled water in which a piece of yeast has been shaken up. If any gas forms within twenty-four hours the yeast is impure.

(*b.*) Distilled water in which some pure grape-sugar and some of the yeast has been dissolved. This is to test whether or not the yeast has fermentative activity. If no gas forms within twenty-four hours the yeast is useless.

[*A rough approximation to the amount of glucose* present may be got by comparing the specific gravity of the urine before the test with the specific gravity taken after it has been fermenting for twenty-four hours. Every degree of specific gravity lost in the process = 1 grain per fluid oz. of glucose.

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* The small amount of CO_2 gas given off in such cases is absorbed by the fluid, and so does not show.

† About 33° C. is the best temperature for this fermentation.

Multiply by the number of ounces passed
in 24 hours = grains of glucose passed daily.

Owing to the fact that practically only glucose produces this reaction, this test is of great value as a *qualitative* test, *if carried out strictly as above directed*, in cases where doubt exists as to the presence of other sugars, or of other interfering substances; but it is much too uncertain and inaccurate for *quantitative* purposes.]

NUMEROUS OTHER TESTS exist for the detection of sugar in urine, but none of them equal those already given. A few of the more noteworthy of the other tests are subjoined, as a knowledge of them is useful, but the three foregoing tests are those recommended for clinical use.

Trommer's Test.—Add cupric sulphate to the albumin-free urine until greenish, and then add liquor potassæ = deep blue. Boil = cuprous oxide ppt. Over-boiling makes the test unreliable. The reduction also occurs with uric acid, mucin, lactose, creatin, creatinin, bile pigments, and when the patient is taking chloral, glycerine, benzoic, or salicylic acids. If less than 2 grains per oz. of glucose be present, this test may fail.

Moore's Test.—To the albumin-free urine add an equal bulk of liquor potassæ, and filter off the phosphates. Then boil the upper layer of the filtrate placed in a test-tube = yellow or brown colour. The test is fallacious, as high-coloured urines, free from sugar, give the reaction which also occurs if rhubarb or senna is being given. If less than 2½ grains per oz. of glucose be present this test cannot be relied on. Another danger is the presence of lead in the liquor potassæ, which may, especially if any albumin is left in the urine, produce a dark sulphide of lead, which may be mistaken for the brown sugar reaction.

Picric Acid Test.—Equal parts of saturated picric acid solution and of liquor potassæ added to the boiling albumin-free urine, give an opaque *orange-yellow to a dark brownish-red colour*. Creatinin, which is present in normal urine, gives a *clear* deep red-blood colour.

To get rid of creatinin, previous treatment with mercuric chloride and sodium acetate is necessary.

Methylene Blue Test.—0·1 grm. (about 1½ grains) of methylene blue is dissolved in 300 c.c. water. Take a few c.c. of this solution in a test-tube, add one-third its bulk of liquor potassæ, and then dilute the whole ten times with water. To this solution add about two c.c. of the albumin-free urine. Boil. If more than ⅓ per cent. of glucose be present, the blue colour disappears.

Böttger's Bismuth Test.—Add to some *albumin-free* urine an equal volume of liquor potassæ, and then add as much bismuth subnitrate as will lie on the point of a *small penknife.* (If too much bismuth be added the reaction may be obscured.) *Boil.* A black ppt. results if sugar be present. This black ppt., which is chiefly formed of metallic bismuth, is due to the *reduction* of the subnitrate by the glucose.

The test has the *advantage* of being a fair "emergency test" as employing reagents to be found everywhere, and it does not react with creatinin or uric acid. Albumin interferes with the test, and reacts like glucose. Its *disadvantages* are those of the other tests which depend on reduction.

When sulphuretted organic substances are present, a black ppt. of bismuth sulphide is formed, which may prove completely misleading.*

GLYCURONIC ACID may be regarded as partially oxidised glucose which on further decomposition yields CO_2 and water. It is present in very small amounts in normal urine but ordinarily in much too small quantity to affect the reduction tests for glucose. It is at once distinguished from glucose by its negative reaction with the fermentation test. It has been observed to precede the onset of glycosuria in certain cases of diabetes. (See also p. 77.) When certain drugs (*e.g.*, morphine, camphor, chloroform, salol, antipyrin, chloral or butyl chloral, benzoic, salicylic or carbolic acids) are being administered the amount of glycuronic acid in the urine may very considerably increase and exercise a pronounced reducing action on Fehling's or other reduction test for glucose.† In such cases the daily quantity of urine passed and the specific gravity will be normal (though the same is occasionally found in mild diabetes—the so-called *Diabetes decipiens*). Glycuronic acid gives the Orcin and Phloroglucin reactions (*see Pentoses*).

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* Nylander's modification (in which bismuth subnitrate is substituted for cupric sulphate in Fehling's solution) is preferable. *Nylander's Solution.*—Bismuth subnitrate, 2 grms.; potassic sodic tartrate, 4 grms.; caustic soda (sp. gr. 1·12), 100 grms.

† When coal-gas has been inhaled in marked quantity, the same result occurs—caused by the nitrobenzene in the gas.

THE PENTOSES are carbohydrates containing five atoms of carbon in the molecule ($C_5H_{10}O_5$) instead of six, as do the hexoses such as glucose, lactose, cane sugar, &c. Pentoses have been found in the urine of morphinomaniacs and beer drinkers (probably from pentoses in beer excreted unchanged); and may also occur along with glucose in diabetes. Pentoses, if taken by the mouth, are not assimilated but are got rid of by the kidneys without suffering change. They respond readily to the reduction tests for glucose, and form an osazone with phenyl-hydrazine. *They are distinguished at once from glucose by means of the fermentation test:* glucose ferments; pentoses do *not.*

I. *Bial's Colour Test for Pentoses*—

Boil 5 c.cs. of urine with 10 c.cs. of Orcin reagent * = greenish-blue colour, which deepens on standing, and later forms a ppt., indicates the presence of pentoses.

II. Pentoses give a cherry-red colour when heated with HCl and phloroglucin.†

Acetone may occur in traces in normal urine but when found in marked quantity in diabetic urine it indicates a severe type and frequently indicates the approach of coma, of which, however, it does not appear to be the cause. It is also found in fevers, carcinoma, pneumonia, nephritis, starvation, and certain forms of dyspepsia.

In pronounced diabetes ·6 to ·8 gramme (8–12 grs.) may be excreted during the 24 hours.

Fehling's solution is reduced by acetone, but this test should be applied to the *distillate* from the urine. Glucose will not distil over but acetone will.

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* *Orcin reagent*:—strong HCl, 500 c.c.; Orcin, 1 grm.; 25 drops of 10 per cent. ferric chloride solution.

† Glycuronic acid gives both these reactions, and is best distinguished from pentoses by separating the glycuronic acid as p. bromphenylhydrazone. This means of distinction is never required clinically, as the fermentation test suffices to distinguish these substances from glucose.

Tests * :—

I. *Legal's Test*—

(*a*.) Alkalinise the urine with liq. potassæ and

(*b*.) Add a freshly prepared aqueous solution (·1 grm. to 15 c.c. of water) of sodium nitroprusside = red colour which disappears.

(*c*.) Then add a few drops of acetic acid = dark violet colour (*Aldehyde* gives an orange-yellow colour with this test).

II. *Lieben*'s *Iodoform Test*—

(*a*.) Add a few drops of liq. potassæ to some of the urine in a test-tube.

(*b*.) Warm gently and add a crystal or two of iodine and shake up = liquid becomes yellow or brownish.

(*c*.) Then add liq. potass. drop by drop till the colour goes = iodoform is pptd. and is recognised by its smell and by its microscopic appearance (hexagonal plates, rosettes, or stars).

[The iodoform reaction is given by aceto-acetic acid, by alcohol—hence a fallacy may occur where glucose is present and has fermented—aldehyde, and some ethers, cane sugar, turpentine, &c.]

Aceto-Acetic Acid.†—When this substance is found in urine it is believed to be always of pathological significance. It occurs in fevers ; and in diabetes its presence indicates a severe case, and often precedes the onset of coma.* It only occurs along with acetone. It is of little use trying to detect it unless the urine is quite fresh.

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* These tests may be applied to the urine without previous distillation but it is far more accurate to apply them to the first few c.c. distilled from the urine. If to be distilled, take about 150 c.c. of urine and acidify with dilute hydrochloric acid before beginning the distillation.

† Hydroxybutyric acid on oxidation yields aceto-acetic acid which in turn decomposes into acetone and CO_2. Acetone and aceto-acetic acid both give the iodoform test but the latter only gives the ferric chloride reaction above described. Aceto-acetic acid produces acetone when heated with liquor potassæ.

Clinically, aceto-acetic acid should be sought for, rather than acetone.

Test :—1. Add some dilute ferric chloride to the fresh urine = ppt. of ferric phosphate.

2. Filter and add a few more drops of ferric chloride = red colour.

Confirmatory.—Divide into two portions (*a*) and (*b*) :—

(*a*) Boil = colour disappears.

To (*b*) add a little sulphuric acid and then a little ether. Separate the ether. Then add some ferric chloride solution and shake up = red colour.

Note.—If, before applying the test, the urine has been boiled no red colour can be obtained.

Antipyrin, carbolic acid, and salicylates give this reaction, but give it also after boiling, which aceto-acetic acid does *not.*

Hydroxybutyric acid (β oxybutyric acid). It is found associated with acetone and aceto-acetic acid in urine and is believed to be always of grave prognostic import in diabetes. The urine in nearly all severe cases of diabetes yields this substance often in large quantity—often as much as an ounce daily may be excreted.† It has also been found in scarlet fever, measles, scurvy, and in certain nervous diseases but has no particular significance attached to its presence in these conditions.

If aceto-acetic acid has not been detected by the ferric chloride test it may be concluded that hydroxybutyric acid is also absent, as these two substances have so far always been found present at the same time, and both react similarly with the ferric chloride test.

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* It is also stated to have been observed in chronic alcoholism, hysterical vomiting, and Graves's disease.

† This acid is one of the most important factors in the production of diabetic coma, not so much as a direct poison, as by lessening the blood's alkalinity too much. The base required to neutralise this acid is got ordinarily from urea, but when any interference occurs with this process, the alkali of the blood is drawn on instead. The blood's alkalinity is reduced, and the consequent defective elimination of carbon dioxide leads to coma.

There is no distinctive test for the presence of Hydroxybutyric acid sufficiently simple for clinical purposes. Külz's method is perhaps the best, but involves distillation, and so is unsuited to clinical requirements.

[Lipæmia, or excess of fat in the blood, is another danger signal, and Frerichs recommends that in diabetics (especially if young) the urine should be examined for Hydroxybutyric acid and the blood for lipæmia every week or two, so that early warning of acidosis may be obtained and alkalies freely administered.]

BILE.—Choluria, or bile in the urine, occurs, speaking generally, when there is any obstruction to the flow of bile through the bile-ducts causing jaundice.

Bile acids and pigments usually occur together, but the pigments are generally in marked excess—at first bilirubin (especially in yellow bilious urines), and later, on standing, biliverdin also (especially in green bilious urines).

Bile pigments are of greater clinical interest as their presence in amounts which react to the tests for them is pathological, while bile-salts are normally present in urine to some slight extent.

Appearance.—Dark yellow to green or dark brown urine with yellow froth on the surface (this distinguishes it from the colour produced by salol). Stains linen or filter-paper markedly.*

TEST FOR BILE-ACIDS, OR, RATHER, BILE-SALTS.

Oliver's Method :—

1. Filter the urine till quite clear,† and if necessary *acidify* (the urine *must* be acid for this test).

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* *Hay's Surface Tension test.*—Sprinkle some flowers of sulphur on the surface of bilious urine = it sinks quickly. When bile-salts are not in excess, the sulphur floats on the surface.

† The urine must be quite clear for this test. If urates be present, heat gently in order to clear. If phosphates, heat and add a drop or two of acetic acid so as to clear. If albumin or blood, boil and filter. (Boiling does not interfere with the reaction.)

2. Add distilled water until the sp. gr. falls to 1008.*

3. Pour gently some of the urine so prepared upon the surface of about one drachm of Oliver's test solution †

= *immediately* a milky disc appears if bile salts be present in excess, which lessens or disappears on shaking, but which reappears on adding more of the reagent.

The ppt. completely dissolves upon adding two or three drops of acetic acid. It diminishes but does not disappear on heating or even on boiling.

(In healthy urine only a very faint thread-like milkiness appears, and that only after some time.)

Oliver's test is exceedingly delicate, but often proves a somewhat uncertain test. It depends on the pptn. of peptone by bile-salts.‡

Pettenkofer's test as applied to urine is often unsatisfactory.

The reaction occurs when the sulphuric acid used is impure (containing oxides of nitrogen or sulphurous acid), and further morphia, albumin and various other substances give the same reaction.

The test is usually conducted by adding strong sulphuric acid and some 10 per cent. cane sugar solution to the urine, and keeping the temperature below 60° F. A reddish-purple colour is produced if the test succeeds.

Instead of this method it is best to dissolve a few crystals of cane sugar in the urine. Then smear some of this mixture on a white plate, and draw through this film a glass rod moistened with pure strong sulphuric acid. If the test succeeds, a reddish-purple streak results.

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* *The addition of water so as* to lower the sp. gr. to 1008 is made in order to lessen the risk of any interference with the test caused by urates or mucin.

† Powdered peptone (Savory and Moore's), 30 grains; Salicylic acid, 4 grains; Acetic acid (B.P.), half a drachm; Distilled water to 8 ozs. Filter till quite clear.

‡ Bile salts in urine are *increased* in liver diseases generally, in leucocythæmia, hæmoglobinuria, pyrexial conditions, malarial anæmia, &c.

BILE PIGMENTS are much more easily detected.

I. *GMELIN'S TEST.*

(*a.*) Filter the urine through white filter paper.

(*b.*) Place a few drops of strong nitric acid in a test-tube, and partly reduce it with a few crystals of cane-sugar or a fragment of granulated zinc (or the same action will result if the acid has been exposed to daylight for sometime so that some nitrous acid has been formed).*

(*c.*) Then with a glass rod place a drop of the acid on the stain on the filter paper=coloured zones,† yellow innermost; then violet-red; then blue; and green outermost.

This method of applying the test is much more delicate than the employment of the "contact-method"—(*i.e.*, by pouring the urine on the surface of the fuming acid in a test-tube).

In case a positive reaction is not obtained with Gmelin's test, and where only traces of bile-pigments are present, *or* where the HNO_3 test for albumin has shown *excess of indican* (greenish-blue colour), then, instead of Gmelin's test, *apply the following*:—

II. *HUPPERT'S TEST.*

(*a.*) Add to the urine lime-water in slight excess;

(*b.*) then add a little ordinary aërated "soda-water" (so that its carbonic acid gas may ppt. excess of the lime) until neutral to litmus paper.

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* This is usually termed *fuming* nitric acid.

† This play of colours is caused by the oxidation of bilirubin in this order: (1) green (bili-verdin); (2) blue (bili-cyanin); (3) violet-red (bili-purpurin); (4) yellow (choletelin). The green colour is characteristic of bile for indigogens may give blue and violet-red reactions with this test.

(*c.*) Filter off the ppt.

(*d.*) Treat it (or even the stain on the filter paper) with *fuming* nitric acid=play of colours as with Gmelin's test.

Confirmatory :—

To another portion of the ppt. add a drop or two of sulphuric acid. *Cool* and then add a small quantity of alcohol.

Boil = ppt. becomes colourless and supernatant fluid becomes green.

N.B.—*Remember that sulphuric acid and alcohol may form an explosive mixture.*

MELANURIA.—In cases of suspected melanotic growths the following tests for melanin may be applied.

Melanin may occur in cases of cachexia (malarial especially) and melanotic tumours, especially of the skin and liver, but, on the other hand, it may be altogether absent in these conditions.

Melanuric urine very rarely exhibits a dark colour when passed but becomes almost black on standing or on adding an acid. It also reacts as follows :—

(1.) With bromine water a yellow ppt. is formed which slowly darkens.

(2.) Again with ferric chloride (strong solution) a *grey colour* results and a ppt. of phosphates and pigment falls. This ppt. is soluble in excess of ferric chloride.

INDICAN.—"Urinary Indican" (potassium indoxyl-sulphate) is present *normally* in small amounts. It appears to be derived from indol during pancreatic digestion, being oxidised to indoxyl and then combining with the alkali and sulphuric acid. It is *normally* increased by a diet richer in meat than in vegetable constituents; by turpentine, strychnia, and prussic acid. It is *much increased* by any cause which partially or completely obstructs the *small* intestine (much less or scarcely at all when the large intestine is obstructed) or by any cause which *increases the putrefaction of proteids.* It has been found increased in phthisis, cancer of the liver or stomach, Addison's disease, oxalic acid poisoning, tabes mesenterica, peritonitis, lymphatic growths, cholera, dysentery, diarrhœa, typhoid fever, and in certain nervous diseases. *It is generally present in relatively large quantity as a normal condition in the urine of persons resident in the tropics.*

When urine containing indican becomes hyper-acid it turns various colours—blue, violet, ruby—usually best seen at the surface of the urine.

DETECTION (on adding HNO_3 in testing for albumin, in many cases a greenish-blue colour may form).

Jaffé's Test:—

1. To about 10 c.c. of urine add an equal bulk of strong hydrochloric acid.

2. Then add, drop by drop, a *saturated* solution of "chlorinated lime" = blue colour ("indigo blue"), and shake up with chloroform. Shake up after the addition of each drop. The chloroform on standing sinks to the foot of the test-tube coloured a more or less deep blue (indigo-blue). The supernatant fluid remains red or purplish.

Indigo-red is formed by boiling some of the urine and then adding a few drops of nitric acid when a red colour results. Shake up with chloroform and it colours the chloroform red.* *If bromides or iodides are being taken* by the patient a similar result may be obtained.

The *quantitative method* is much too complicated for clinical use.

EHRLICH'S DIAZO REACTION is ordinarily present in well-developed attacks of typhoid fever, though in mild attacks it may be absent. It is also found in rapidly progressing tuberculosis of the acute miliary form—during and after the third week; *occasionally* in malarial fevers, measles, scarlet fever, erysipelas, and pyœmia.†

TEST.—The following two reagents *must be freshly prepared*:—

(*a*.) Sulphanilic acid (saturated solution) to which is added 5 per cent. of hydrochloric acid.

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* *Ururosein* is a urinary chromogen which reacts similarly, *but is not soluble in chloroform* like indigo-red.

† It used to be supposed that this reaction did not occur in German measles (Rubella), but this view is apparently no longer tenable.

(*b.*) A half per cent. solution of sodium nitrite.

(1.) To a small quantity of urine in a test-tube add an equal volume of sulphanilic solution (*a*) and then three or four drops of the nitrite solution (*b*) and *shake vigorously.*

(2.) Alkalinise with ammonia = liquid *and froth* turn a *dark-red colour.*

Rationale.—When sulphanilic acid (amido-sulpho-benzol) is acted on by nitrous acid, diazo-sulpho-benzol forms which, in the presence of certain aromatic substances markedly present in the urine in the above-mentioned conditions, produces a red (aniline) colour.

UROBILIN, see page 146.

PTOMAINES AND LEUCOMAINES.

The methods for the separation of these substances can only be carried out in a well-equipped laboratory so that it would be useless to describe them in a work intended only for clinical and class purposes.

DRUGS IN URINE.

1. *Acids*—see Vegetable Acids.

2. *Alcohol* when taken in marked excess may appear in urine as very faint traces.

3. *Alkalies and alkaline carbonates* alkalinise the urine.

4. *Alkaloids* (Atropine, Strychnine, Quinine, and Morphine) may be excreted unchanged except Morphine, which is *in most cases* completely broken up in the system. Animal alkaloids are also excreted in the urine.

5. *Antifebrin is detected in urine by*—

(*a.*) Adding to the urine a few drops of strong Sulphuric Acid;

(*b.*) Boil; (*c.*) Cool and add a few drops of Calcium hypochlorite, and then a small quantity of HNO_3 = red, later becoming blue.

6. *Antipyrin* may give the urine a red colour somewhat resembling blood.

(1.) Add neutral ferric chloride = purple-red colour. Boil = no change.

(2.) Partially reduces Fehling's solution.

(3.) With Tanret's reagent gives a ppt., *sol. on heating.* With HNO_3 test = *no ppt.*

7. *Arsenic*—Reinsch's process.

8. *Benzoic Acid* appears in the urine as Hippuric Acid (examine under microscope for the crystals).

9. *Bromides*, if in large amount, may be sought by the addition of hydrochloric acid and dilute solution of "bleaching powder." On shaking up the solution with chloroform = brownish-red colour from free Bromine. Bromides and Iodides cause the urine to darken when nitric acid is added to it.

10. *Carbolic Acid* colours the urine dark-brown to green or greenish-black. Add some Bromine water "suddenly" to some urine in a test-tube = evanescent opalescence or when present in large amount a yellowish-white ppt. (tribromophenol).

11. *Chloroform or Chloral.* The urine will contain Glycuronic acid as a "paired" compound—*e.g.*, urochloralic acid with chloral hydrate, and will, therefore, reduce Fehling's solution. It will also give with Phenyl-hydrazine a brown ppt. The *acid* urine, however, if treated with Yeast will not ferment as when Glucose is present.

12. *Gallic and Pyrogallic Acid* appear as such and as pyrocatechin, &c.

13. *Iodides.* Add a little nitric acid; shake up with chloroform (carbon bisulphide, if available, is preferable) = red colour. (Iodides, Bromides, and Chlorides of Potassium and Sodium appear in urine practically unchanged. Iodine appears as an *iodate.*)

14. *Iodoform.* Shake up with ether, which is separated and evaporated when Iodoform separates. (Odour and hexagonal or rosette crystals under microscope.)

15. *Lead.* In plumbism it is necessary at times to ascertain the presence or amount of lead being excreted by the urine.

In testing for lead first ascertain that the reagents used are free from lead.

The presence of lead may often be detected by simply dipping a piece of white filter paper into the solution (or urine) and then dropping some recently-prepared sulphuretted hydrogen solution on the stain = black stain if lead is present.

The better way to proceed, however, is to—

(1.) Pass H_2S gas through the solution or urine = black ppt.
(2.) Filter and wash the residue on the filter with distilled water.
(3.) Collect the residue and boil for 15 minutes with 20 per cent. HNO_3.
(4.) Filter.
(5.) Evaporate filtrate to dryness.
(6.) Redissolve in water.
 (*a.*) To one portion add a little Sulphuric acid = white ppt., which dissolves in Caustic Potash.
 (*b.*) To another portion add Ammonium Sulphide solution = black ppt.

16. *Mercury.* Reinsch's process.

17. *Morphine* requires extraction by processes which cannot well be conducted outside a chemical laboratory.

18. *Phenacetin.* Acidulate urine with strong HCl and heat. Cool and add a few drops of ferric chloride = reddish-brown colour.

19. *Quinine*—

(1.) To 10 c.c. of urine add a drop of strong Hydrochloric acid.
(2.) Then a few drops of recently-prepared Chlorine water.
(3.) Then add excess of Ammonia solution = emerald-green colour.
 Confirm—Neutralise the solution with HCl = blue colour.
 Add excess of acid = purple or red colour.
 Add excess of ammonia = green colour.

20. *Salol or Salicylates* appear as salicyluric acid in the urine, which may be coloured dark-green or greenish-black, and which further reduces Fehling's solution. Add neutral ferric chloride solution = blue-violet colour, if large amount present. If even very small quantities are present, acidulate with sulphuric acid. Cool. Agitate with equal bulk of ether. Separate the ether and add ferric chloride = blue-violet colour.

21. *Santonin* may simulate bile by colouring the urine a greenish-yellow. It generally produces an *orange* colour.

Add some Liq. Potassæ = purplish-red colour, *which quickly disappears.* (Chrysophanic Acid gives a purple-red colour *which lasts for some time.*)

22. *Senna or Rhubarb* may give the urine a brownish or orange colour, *chrysophanic acid being produced.*

Add Liq. Potassæ = becomes purplish-red, which lasts for some time.

Add hydrochloric acid = red colour disappears.

23. *Metallic Compounds*—arsenic, antimony, mercury, copper, silver, lead—appear in the urine in traces. The first three mentioned may be detected by Reinsch's process and the others by applying to the ash the ordinary tests for silver, copper, or lead.

24. *Rosanilin* colours the urine red. Alkalinise with ammonia. Shake up with ether, pour off the coloured ether layer and place some white cotton threads in it. They are dyed red.

25. *Sulphur* appears as sulphates in the urine.

26. *Tannic acid* is mostly transformed into gallic acid in the urine. With ferric chloride such urine gives a dark green colour.

27. *Urotropin* is excreted as *formaldehyde.* This latter powerfully reduces Fehling's solution, and when treated with equal parts of Phenyl-hydrazine hydrochloride and Sodium Nitroprusside, and then with *excess* of liquor potassæ = *dark-blue colour.*

28. *Vegetable acids* generally appear in the urine as carbonates. *Acids in general* (but especially *mineral*) pass into the urine as salts and tend to increase somewhat the acid reaction given by urine. *When the patient is taking mineral acids it may be necessary before testing for albumin to reduce the acidity of the urine somewhat* (*by adding some liquor potassæ*) *to prevent the formation of acid-albumin.*

PART II.

QUANTITATIVE METHODS.

PART II.

QUANTITATIVE METHODS.

PRELIMINARY REMARKS.

THE quantitative methods which follow are divisible into three groups :—

I. Gravimetric Processes in which the constituent to be estimated is separated in a sufficiently pure state (or as some new compound of known composition) and then weighed on an accurate balance. A chemical balance is, however, rarely available for clinical work so, as far as possible, methods have been described which do not require its use.

This is one of the methods described for estimating :

(*a*.) Albumin ;
(*b*.) Uric acid ;
(*c*.) Oxalates.

II. Volumetric Processes in which solutions of known strength are made to react with one another and from the *volume* needed to produce the reaction the weight of the substance sought is determined.

This method is particularly convenient as there is no obligation to obtain the substance which is being estimated in the pure condition, as the presence of other substances does not interfere with the "*end-reaction*"—*i.e.*, the change of colour which shows the completion of the process. Furthermore, it dispenses with the need for a chemical balance and is besides, generally, a more rapid method than a gravimetric process.

In order to obtain accurate results with volumetric processes the solutions employed *must be carefully standardised before use* in order to make sure that they are of the requisite strength.

To expect the medical practitioner to do this is to expect too much, for he has neither the time nor the appliances to do so.

It is best therefore for him to obtain the requisite solutions already carefully standardised from a reliable firm of chemists.* If for any reason this is impracticable the only alternative will be to prepare the solutions *in strict accordance with the directions herein given and with ingredients which are, as far as possible, chemically pure.*

The hypobromite solution for urea, however, cannot be obtained from chemists as it *must* be prepared fresh just before use.

The copper and the alkaline tartrate solutions which when mixed constitute Fehling's solution must be *mixed immediately before use.*

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* The following firms have arranged to supply all standardised solutions referred to in this book :—

London—Baird & Tatlock, Cross Street, Hatton Garden.
Edinburgh—Alex. Fraser, 22 Teviot Place.
Calcutta—Smith, Stanistreet & Co., Chemists.
Bombay—Kemp & Co., Chemists.

The Volumetric processes described in the following pages are as follows :—

(*a.*) Glucose by Pavy's or Fehling's methods.

(Here the solution ought to be standardised by means of a solution of grape-sugar of the requisite strength.)

(*b.*) Urea by means of hypobromite solution

(MUST BE PREPARED JUST BEFORE USE).

(*c.*) Uric acid by a piperidine solution standardised against a $\frac{1}{20}$th normal acid solution; or by a permanganate solution standardised against a potassium nitrite solution.

(*d.*) Phosphates by a Uranium nitrate solution standardised against a phosphoric acid solution of the necessary strength.

(*e.*) Chlorides by a solution of Silver Nitrate standardised against a Sodium Chloride solution.

(*f.*) Total acidity by a Caustic Soda Solution standardised against an Oxalic Acid solution.

III. POLARIMETRY.

This is an alternative method recommended for estimating glucose, the amount of which can thus be *directly* determined. It is specially suitable for hospitals, or where a large number of samples have to be examined.

In the following pages special attention has been directed to the selection for description of those processes which are not only the simplest and most rapid, but which are, at the same time, quite sufficiently reliable for all ordinary clinical purposes. A choice is generally given, on the one hand, of a short method sufficiently approximate in its results for most clinical requirements, and also of another more elaborate process which will give more accurate indications for cases where a higher degree of accuracy is requisite.

Thus for Albumin, Sugar, Urea and Uric acid *alternative* processes are given, as these substances are those most often estimated in urine. For Chlorides, Oxalates, Phosphates, Total Solids, and Total Acidity, which are estimations rarely required, one process of sufficient accuracy for clinical needs is described.

ALBUMIN.—In albuminuria, the quantity present is usually well under 1 per cent., but may even amount to 4 per cent. (or, it is stated, to 5 per cent., which is the proportion found in blood serum).

For *the quantitative estimation of albumin by means of Esbach's tube* the urine must be—

(*a.*) Fresh and clear;

(*b.*) Below 1010 in sp. gr.; and

(*c.*) Should contain not less than 0·05 per cent. or not more than 0·5 per cent. of albumin, otherwise the indications are untrustworthy.

Method.—Esbach's solution is prepared by dissolving $\frac{1}{4}$-oz. of Picric Acid and $\frac{1}{2}$-oz. Citric Acid in 25 ozs. of boiling water. Cool.

(*a.*) If the sp. gr. is high, or if albumin by the qualitative tests appears to be present in particularly large amount, the urine must be diluted until the sp. gr. falls below 1010, *carefully noting the bulk of water added.*

(*b.*) Then fill the Esbach tube (which is merely a specially graduated thick test tube) up to the mark U with the filtered *acid** urine, previously diluted if necessary;

(*c.*) Then add the Esbach's solution up to the mark R on the tube;

(*d.*) Cork and *gently invert* (*without shaking*) the tube several times so as to mix thoroughly;

---

* If alkaline, acidify with dilute Acetic acid.

(*e.*) And then place upright for 24 hours;*

(*f.*) Then read off the figure on the tube corresponding to the upper surface of the ppt.

Each degree = $\frac{1}{10}$th per cent. of albumin.

(*g.*) *If the urine has been diluted with water, multiply the reading of the tube by the number of volumes of water used.*

(*h.*) If the reading of the tube is 5 or above *with undiluted urine*, then repeat the operation after diluting the urine with once or twice its volume of water.

If, instead of as a percentage, *the result is required in grains per ounce*, multiply the tube's reading (corrected, if necessary, for dilution) by 4·375 (or, roughly, by $4\frac{1}{2}$).

To obtain the daily loss of albumin—

(*a.*) Multiply the percentage by $4\frac{1}{2}$;

(*b.*) Then by the number of ounces of urine passed in the 24 hours = grains of albumin passed *per diem.*

Note.—The tube is graduated on the understanding that the ppt. will be allowed 24 hours to settle, and it is also graduated at 15° C.

But the separation of the ppt. can be effected in a few minutes by means of a centrifuge.

The figures on the tube correspond to grammes of dried albumin per litre (1000 c.c.). The percentage is got by simply placing a decimal point before the figure.

Example.—If the ppt. reaches the mark 2, that is ·2 of a gramme in 100 c.c., or $\frac{1}{5}$th per cent.

If the ppt.'s surface lies between any two figures, then roughly measure the distance from the lower figure—*e.g.*, $\frac{1}{2}$, $\frac{1}{3}$, &c.

If, for example, the ppt. reached midway between figures 2 and 3 = ·25 per cent. of albumin.

Caution.—Uric acid and coloured urates if pptd. are distinguished from albumin by the colour and the amount of coloured ppt. must be deducted from the space occupied by the pptd. albumin.

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* Variations of temperature cause marked variations in the amount of ppt. *Therefore, stand the tube in a place where the temperature remains about the same during the 24 hours.*

The above method is ordinarily sufficiently exact for clinical purposes, and is of course vastly superior to the old method of letting the ppt. produced by boiling separate, and then noting the relative amount present—*e.g.*, ¼th, ⅓rd, &c.*

The late Prof. Sir T. Grainger Stewart, of Edinburgh, and the late Sir George Johnson, of London, found that Esbach's method *gave practically the same results* as the gravimetric method. Graaf found that the results obtained by polarimetry did not vary more than ·1 or ·2 per cent. from the Esbach method.

But the method is always open to the objection that alkaloids, albumose and light-coloured urates are also pptd. by the picric acid. It yields, further, only comparative, not absolute, results.

QUANTITY PRESENT OF ALBUMIN IN VARIOUS DISEASES :—

Large amounts of albumin are generally found in acute nephritis (especially post-scarlatinal), also in "*large pale kidney*,"—*i.e.*, a high *percentage*, but the total amount may be often relatively small because the quantity of urine is diminished. In subacute and chronic forms of nephritis, the amount is very variable. In *granular and waxy kidney*, the *percentage* may be less, but more albumin may be lost as polyuria exists. As much as 40 grammes daily of albumin may be lost in these conditions. In *waxy kidney* the amount is at first small, but increases much later. In *cirrhotic kidney*, small amounts or none at first; and all through the disease albuminuria is apt to intermit. Albumin even may not be found for several days at a time. The polyuria present lowers the percentage found as a rule. The amount of albumin is generally small in *active and passive renal congestion.* In *infarction of the kidney* albumin suddenly appears often in large amount, and at times as suddenly disappears. In various forms of nephritis the quantity of albumin is frequently found to increase on sudden alteration of the diet, whether this is made more liberal or more sparing. Anxiety also markedly increases the amount of albumin.

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* With this old method confusion of *percentage by bulk* with *actual* percentage was common. When, for instance, the ppt. amounted to ⅓rd of the column of urine in the test-tube, it was often supposed that this meant over 33 per cent. of albumin—the *actual* amount present being perhaps 1 per cent.

[Where a Laboratory is Available the most accurate method of all for estimating the total proteids in urine is by the following gravimetric process :—

(*a.*) Take a measured amount of the urine and add five times its volume of *absolute alcohol ;*

(*b.*) Set aside for some hours ;

(*c.*) Then collect the ppt., and wash with hot alcohol and ether ;

(*d.*) Dry ; and weigh.

(*e.*) Then incinerate to get the ash and deduct the ash from the weight got at (*d*) = amount of total proteids present.]

GLUCOSE.

[The Fermentation test used to be a favourite method for estimating glucose, but is not only too tedious but much too inaccurate in its results. If should certainly not be employed *for quantitative purposes.*]

The Copper Methods are the most useful and give sufficiently approximate results for ordinary clinical purposes if carried out carefully as described hereinafter. Either the ordinary Fehling method, or Pavy's modified Fehling method may be employed.* The ordinary Fehling method (when carefully employed) gives sufficiently exact results for most clinical purposes, and is undoubtedly the simplest and most convenient method of any, as well as being the process in most frequent use in this country.

THE ORDINARY FEHLING TEST gives good approximate results with fresh urine so long as

(1.) *The urine is not ammoniacal,* for then the ammonia dissolves up the cuprous oxide as soon as it forms; and

(2.) *When not more than one per cent., or less than a half per cent. of glucose is present.* In order to fulfil this requirement, the urine must be previously diluted to the required extent.

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* The previous removal of such reducing substances as uric acid, creatinin, &c., by means of pptn. with mercuric chloride and sodium acetate, and the subsequent treatment with zinc dust and ammonia (necessary to remove the mercury) while greatly adding to the accuracy of the process occupies more time than can usually be spared in making clinical estimations. As a matter of practice in large hospitals and clinical laboratories this preliminary treatment is omitted.

(3.) *The urine must be freed from albumin* by boiling the acid urine and filtering.

METHOD :—

(*a.*) From the sp. gr. some idea will have been formed as to the amount that it will be necessary to dilute the urine before starting the estimation. This may be from 4 to 20 times its bulk, the diluent being freshly-boiled water. *The higher the sp. gr. the more water is to be added.* For ordinary diabetic urine, generally 9 parts of water to 1 of urine is sufficient. Of course, note carefully the volume added.

(*b.*) Now pour the diluted urine through a funnel into a 25 or 50 c.c. burette, fitted with a ground-glass stopper. Fill the burette to the top, then open the stopper and run off the urine down to the zero mark on the burette.

(*c.*) Mix the alkaline tartrate solution with the cupric sulphate solution in equal parts (*vide* p. 85).

(*d.*) Then place 10 c.c. of this Fehling's solution in a porcelain capsule, and add 40 c.c. of recently boiled water to it.

(*e.*) Place the capsule on a piece of wire gauze placed on a tripod stand (or clamped retort ring), and *boil before adding any urine* to see that the Fehling solution has not deteriorated by keeping (add a few pieces of fresh pumice-stone to the solution to prevent "bumping").

(*f.*) Then place the burette over the capsule and gradually run in the diluted urine, *continuing to gently boil the Fehling's solution while so doing* until the blue colour has almost disappeared. *A yellowish-red ppt. of cuprous oxide will also form,* which must be allowed to settle occasionally by stopping the addition of urine and by removing the flame for a few seconds.

(*g.*) Then continue the addition of the urine *drop by drop* till all the blue colour is discharged, tilting the capsule so as to get the white surface under the fluid, and so be able to judge more accurately the point at which it becomes colourless. Observe this before allowing the deposit to completely separate, as the oxygen of the air causes a slight return of the blue colour.

(*h.*) *In order to be quite sure that all colour is discharged—*

(i.) Filter a few drops into a test-tube, *and*

(ii.) Then dip a glass rod moistened with acetic acid into it, and mix with a drop of potassium ferrocyanide solution on a white plate.

If a red-brown colour follows, go on with the addition of urine. Continue the addition of urine *until no colour results with the ferrocyanide solution.*

(*i.*) Read off the number of c.c. of the diluted urine used and calculate as under.

NOTE.—*It is always wise to repeat the whole experiment.*

Calculation.—Suppose that 5 c.c. of urine have been diluted with 45 c.c. of water, and that the whole amount (50 c.c.) has been used to completely ppt. the copper in 10 c.c. of Fehling's solution.

10 c.c. of Fehling's solution = ·05 grm. glucose. Therefore the 5 c.c. of urine also = ·05 grm. glucose.

How much would this correspond to in 100 c.c. of urine?

$$\frac{100 \times \cdot 05}{5} = 1 \textit{ per cent.}$$

Now multiply the percentage figure by 4·375 to bring to grains per oz.—*i.e.*, 1 × 4·375 = 4·375 grs. of glucose per oz.

The daily amount of glucose is obtained by multiplying the grains per oz. by the total number of ozs. of urine passed during the 24 hours.

Pavy's Modified Copper Process.

Pavy's process should be used:—

1. *When the urine is ammoniacal, or not fresh,* and is
2. Much better than the ordinary method *when small amounts of glucose or large amounts of extractives or of ammonio-magnesium phosphates are present.*

The process depends on the fact that the cuprous oxide produced by the reducing action of the glucose is kept in solution by the ammonia, and is not pptd., as in the ordinary Fehling's process. When all the copper has been reduced, the liquid therefore becomes quite colourless, and the reaction is finished.*

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* Both Pavy's and Fehling's methods are affected to some slight extent by uric acid, if present, but the slight error from this is for clinical estimations negligible.

Pavy's ammoniacal cupric solution is made by mixing 300 c.c. of "ammonia solution" of ·88 specific gravity with 120 c.c. of Fehling's solution (*vide* page 85) and then adding 100 c.c. of caustic soda solution (10 per cent. strength). Then make up to one litre with distilled water. The resulting colour is darker than that of ordinary Fehling's solution.

1. The test is conducted as in the preceding method, but in Pavy's process the point which marks the completion of the process ("end-reaction") *is the disappearance of all blue colour.* The end-reaction is much sharper in Pavy's method.

2. *No yellowish-red ppt. forms*, as the cuprous oxide is dissolved up as quickly as it forms by the ammonia present.*

3. The urine must be added much more slowly, as the reduction is slower than in the ordinary Fehling's test—*about a drop a second is safest.*

4. Do not forget that 10 c.c. of Pavy's solution correspond only to ·005 grm. of glucose (not to ·05 grm. as in ordinary Fehling's solution). *Bearing this in mind*, the calculation is the same in both. (An example of the calculation with Pavy's method is, however, given further on.)

The following precautions are necessary in order to exclude air, *as the blue colour returns very rapidly on*

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* If the boiling is too prolonged, as shown by the occurrence of a brick-red ppt., repeat the process. Be careful to clean the flask thoroughly, using a small amount of dilute HNO_3 to dissolve any adherent ppt.

exposure to air, and to lessen the annoyance from the ammonia fumes* :—

(*a.*) Place 50 c.c. of the copper solution, diluted with 50 c.c. of water, in a GLASS FLASK *fitted with a rubber cork in which two holes are bored.*

(*b.*) Through one of these holes passes a piece of glass-tubing connected by means of a piece of rubber tubing with the nozzle of the burette containing the diluted urine.

(*c.*) Through the other hole in the cork passes a straight piece of glass-tubing about 2½ feet long, and open at both ends. This is to carry off the ammonia fumes produced.† The process ought to be conducted in a current of air so as to remove the ammonia escaping from the tube.

(*d.*) Be careful to boil all the air out of the flask before beginning the addition of the urine. Keep the solution boiling while running in the urine.

Boil the flask on a square of asbestos in the centre of which a round hole (1½ inches in diameter) has been made to admit the flame. The white surface makes it easier to note the complete disappearance of the blue colour.

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* By employing Gerrard's cyano-cupric process ammonia-production is avoided, and the process can be also conducted in an open vessel. But otherwise the process presents no advantages over Pavy's method, and has not been sufficiently worked out as regards the effect of the other urinary reducing substances.

† Instead of this long glass-tube, a piece of rubber-tubing may be attached to a short glass tube piercing the cork. This tubing may then be made to end outside a window.

Example of Calculation with Pavy's Process.

(*a.*) 50 c.cs. of Pavy's solution were taken and correspond to ·025 grm. glucose—(*i.e.*, 10 c.c. Pavy = ·005; and 50 c.c. = ·025).

(*b.*) Suppose the urine was *diluted* 1 in 10 and that 9·5 c.c. were needed to decolourise the 50 c.c. of Pavy's solution :—

i.e., 9·5 c.c. = ·025 grm. of glucose.

(*c.*) But 9·5 c.c. of the *diluted* urine (1 in 10), = ·95 of the *undiluted* urine—*i.e.*, ·95 c.c. of the urine = ·025 grm. glucose.

(*d.*) How much will 100 c.c. of urine contain?

$$\cdot 95 : 100 :: \cdot 025 : x.$$

(*e.*) Multiply x by 4·375 to bring to grains per oz.

(*f.*) Multiply grs. per oz. by total number of ozs. passed during the 24 hours to obtain the daily excretion of glucose.

POLARIMETRY.

By the use of the Reichert-Ultzmann's Polarising Saccharimeter the percentage of glucose in urine can be rapidly and very easily ascertained, and so long as over ·5 per cent. of glucose be present the results are fairly accurate. Where many samples of urine have to be examined quantitatively for sugar, as in hospitals or clinical laboratories, this method is very convenient.

Glucose in solution rotates the polarised ray to the right (dextro-rotatory).

Hitherto it has been found very difficult to employ the polariscope for clinical purposes, but Ultzmann's instrument is not only comparatively inexpensive (about £4) but can very easily be adjusted on an ordinary microscope stand by simply removing the microscope's eye-piece, objective and tube, and fixing the saccharimeter in its place. No artificial illuminant is necessary. The instrument* consists of :—

(j.) An eye piece in which is enclosed a Nicol's prism connected with a graduated scale and vernier and between the prism and the eye are placed a biconcave lens and an objective with a focal distance reaching as far as the quartz plate in the lower objective tube (iij.).

(ij.) A glass tube (in which the urine is placed) fits between (j.) and (iij.).

(iij.) The lower objective contains a second Nicol's prism and a double quartz plate capable of rotating light to the right or left.

The scale close to the eye-piece is graduated so that each division corresponds to one per cent. of glucose at 20° C. and by the vernier tenths of a degree can further be read.

METHOD OF EMPLOYMENT.

(1.) First set the instrument to zero by filling the tube (ij.) with distilled water, placing it in position, and then observing if the field of vision *is of the same tint throughout* and if the *scale and its vernier mark zero.*

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* A description of the polarimeter and the principles of polaroscopy may be found in any standard work on Physics.

If not, adjust to zero. This need only be done from time to time to see that the instrument is working well. Ordinarily proceed straightway to fill the tube with the urine to be examined (clarified if necessary).

(2.) Then fill the tube with the urine to be tested.

[The urine unless quite clear and practically colourless (as diabetic urine often is), must be clarified by—

(*a.*) Mixing 75 c.c. of urine with 25 c.c. of a solution of equal parts of Acetate of Lead and of Alum (both of 10 per cent. strength), and then

(*b.*) Filter off the resulting ppt. of albumin, uric acid, phosphates, pigments, sulphates.]

The tube must be filled almost to over-flowing, and then the cover-glass is pushed on side-ways *so that there are no air bubbles left in the tube.*

(3.) Then place the tube in position, and observe that the field is now (*i.e.*, if glucose be present) *unequally* tinted.

(4.) Turn the vernier by the screw until the tint is the same throughout the field, and read off the percentage of glucose.

(5.) As the urine was diluted with the alum and lead acetate solution, multiply the reading by 1·33, *and this gives the percentage of glucose present.*

The polarising test may be interfered with by the co-existence of Glycogen, levulose, and milk-sugar (lactose).

Glycogen is dextro-rotatory. It does not reduce Fehling's solution or ferment with yeast.

Lactose is also dextro-rotatory. It does not ferment with yeast.*

Glycuronic Acid as it occurs in urine deflects the polarised ray *to the left.*

Levulose may occur along with glucose in diabetic urine. The polarised ray is markedly deflected *to the left.* Levulose ferments with yeast like glucose.

Pure *Cane-sugar* is dextro-rotatory, but commercial samples of cane-sugar have nearly always a small amount of *glucose* mixed with them. It does not react to the Fehling, Safranine, or Phenylhydrazine tests.

Inosite has no optical activity.

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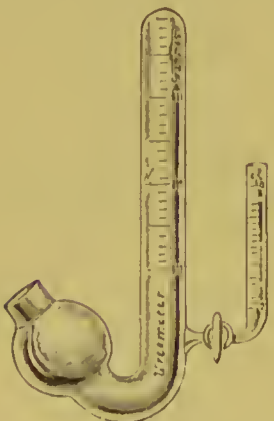
* See also p. 87.

UREA is most conveniently estimated by Hüfner's Hypobromite method, which is not only easier but more accurate than Liebig's mercuric nitrate process.*

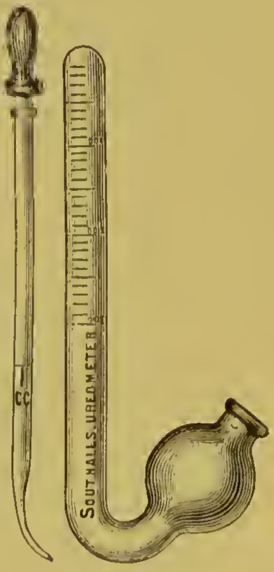
HÜFNER'S METHOD. — The amount of urea is calculated from the amount of nitrogen gas evolved from it by the action of alkaline Sodium Hypobromite solution.†

Water and carbonic acid are the other products of this reaction, but their presence does not interfere with the nitrogen result in any way, as the carbonic acid combines with the soda. From the nitrogen the urea is calculated on the basis of ·1 gramme of urea yielding 37·2 c.c. of nitrogen at 0° C. and under 760 m.m. pressure.

Various ureometers are in use, but the simplest and most convenient is that of Dr. Doremus of New York, (modified by Southall). The best form of this instrument is Hind's modification (see figure), as it does away with the inconveniences inseparable from the use of the pipette,



HIND'S MODIFICATION OF THE DOREMUS TUBE.



SOUTHALL-DOREMUS TUBE.

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* Perhaps the most accurate method of all is Mörner's and Sjöquist's, but it is solely a laboratory method, and so quite inapplicable to clinical purposes.

† Hypo*chlorite* of Sodium or Calcium may also be used. In hot climates especially "chloride of lime" (which is required in the preparation of Sodium Hypochlorite) very rapidly deteriorates, and hence the Hypobromite is much preferable on this account, and because of the comparative ease with which it can be prepared.

the nipple of which is also very liable to crack and become leaky and unserviceable, or lose its elasticity in course of time.

I. ESTIMATION BY DOREMUS'S UREOMETER.

As will be seen, the apparatus is a bent tube with a long limb closed at the top, and with a short limb on which is an open-mouthed bulb. A 1 c.c. pipette with a rubber-nipple is also supplied with the apparatus, but Hind's modification, in which the urine is run in from a side tube, is preferable.

The *Hypobromite Solution* is prepared by dissolving 100 grammes of caustic soda in 250 c.c. (or 6 ounces of NaOH to a pint) of water. Cool and then take 25 c.c. of this solution and mix with 2·5 c.c. of Bromine.

It must be freshly prepared on the day of the estimation as it decomposes when kept—*i.e.*, the caustic soda solution can be kept in a stock bottle but must not be mixed with the Bromine until the test is to be applied.

CAUTIONS AS TO PREPARING THE HYPOBROMITE SOLUTION.

(*a.*) Bromine and *not Bromine water* must be used. AS BROMINE IS A VERY POWERFUL CAUSTIC, CARE MUST BE TAKEN WHEN WORKING WITH IT.

(*b.*) Pour the Bromine into the solution by means of a funnel whose lower end dips into the solution, *and add only one or two drops of Bromine at a time*, stirring with the funnel while doing so.

(*c.*) It is much safer, in order to avoid violent action and spirting of the Bromine, to surround the bottle into which it is poured with *very cold water.*

METHOD.

(1.) Fill the apparatus with the hypobromite solution by pouring it into the bulb and then tilting the long limb so as to fill it to the bend at the bulb, leaving the bulb almost empty. (Often there is a mark on the bulb to show the point to which the hypobromite solution is to be added.) If Hind's apparatus is used, see that the stop-cock is closed so as to cut off the side tube.

IF HIND'S APPARATUS IS USED—

(2.) Fill the side tube (which is graduated in tenths of a c.c.) with urine up to the 0 mark (the urine must have previously been *freed from albumin* by boiling and filtration).

(3.) Then turn the stop-cock and *very slowly* run in *exactly* one c.c. of the urine.

IF THE NIPPLE-PIPETTE IS TO BE USED—

(1.) Fill the 1 c.c. pipette with the urine (*previously freed from albumin by acidulation, boiling, and filtering*) up to the 1 c.c. mark. Then wipe the pipette dry.

(2.) Then push the nozzle of the pipette as far as possible up the long limb of the ureometer and very slowly eject *the whole contents* of the pipette.

(3.) Withdraw the pipette, *keeping the rubber-nipple tightly squeezed while doing so or fluid will be sucked up into it.*

After about quarter of an hour read off the amount of gas which has collected in the long limb, which is scaled empirically—

(*a.*) In grains per fl. oz. of urine;
(*b.*) Metrically;
(*c.*) Or in both (*a*) and (*b*).

If the instrument is metrically scaled then the large divisions are centigrammes of urea per c.c. of urine, and the smaller divisions correspond to milligrammes. If, then, the reading be ·015, that means ·015 in 1 c.c. of urine, and so, on multiplying by 100 = 1·5 per cent. of urea.

If the amount of gas is sufficient to depress the fluid beyond the limits of the graduated scale then repeat the experiment, using ·5 c.c. of urine mixed with ·5 c.c. of water, and multiply the result by 2.

TEMPERATURE.

If the temperature of the room is *about* 65° F., no correction for temperature need be made.

But in hot climates where the temperature may be very much higher, the long tube must be wrapped in a piece of muslin *wetted with iced water*. By this means the contents can be cooled to about 65° F., and this will be shown by placing a thermometer in the fluid in the bulb of the apparatus.

It is quite unnecessary for ordinary approximate clinical purposes to make the corrections for pressure and tension of aqueous vapour.

The main objection to the Doremus apparatus is that only 1 c.c. of urine is operated on, and this cannot be expected to give very exact results, but this loss in accuracy does not amount to much.

Other objections are that some of the nitrogen evolved may escape round the bend of the tube; that urea is not the only nitrogenous substance indicated by the test; and especially that where glucose coexists in the urine, the amount of nitrogen is increased (because of the heat evolved by the interaction of glucose and the hypobromite).

In spite, however, of these objections, the method is almost universally employed in hospitals and in private practice as the simplest and readiest means of estimating urea, and as yielding sufficiently approximate results for clinical requirements.

II. ESTIMATION BY DUPRÉ'S METHOD.

Where much more accurate results are required, a *Gerrard's or Dupré's* ureometer ought to be employed. The latter may be improvised—

(*a*.) Take a glass burette of 50 c.c. capacity which is graduated (as they generally are) to $\frac{1}{10}$th of a c.c. Close the stopcock, and fix (with thin wire) a piece of rubber tubing to the nozzle.

(*b*.) This rubber tubing is then attached to a piece of glass tube passing through the cork of a small glass flask.

(*c*.) The burette is *inverted* and fixed (by a clamp) in a glass cylinder filled with water, so that it can be raised or lowered at will in the water.

METHOD.

(1.) 25 c.c. of the Hypobromite solution are placed in the glass flask.

(2.) A *miniature* test-tube is filled with 5 c.c. of albumin-free urine, and is then carefully placed by means of forceps in the flask, taking care that none of its contents are spilt while doing so.

(3.) Cork the flask.

(4.) Then *open* the burette's stop-cock, and lower the burette in the cylinder of water until the zero mark is reached.

(5.) Now *close* the stop-cock, and then see that the burette is air-tight by raising and lowering it a little; and, if no leakage is found, then finally lower it again to the zero-mark.

(6.) Open the stop-cock of the burette, and tilt the flask so as to upset *all* the urine into the hypobromite solution. Then place the flask in cold water. The gas passes into the burette and depresses the level of the fluid.

(7.) Wait for fifteen minutes until all effervescence has ceased.

(8.) Then raise the burette till the level of the water in it corresponds with that in the cylinder.

(9.) Read off the number of c.c. of gas formed. *Correct for temperature, pressure, and tension of aqueous vapour:* and then calculate on the basis that 35·4 c.c.* of nitrogen correspond to 0·1 gramme of urea. (*In diabetic urine* 37·2 c.c. of nitrogen = ·1 grm. of urea.)

USE THE FOLLOWING FORMULA :—

$$V' = \frac{V \times (B - T)}{760 \times (1 + 0{\cdot}003665t)}$$

V′ = Correct volume ; V = Observed volume.

B = Height of barometer (this need not be corrected for temperature for our present purpose), but remember to convert the inches of the barometric reading into millimetres by multiplying the reading in inches by 25·399 (1 inch = 25·399 m.m.).

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* Theoretically 37·27 c.c. should be obtained, but practically it is found that 35·4 c.c. only are obtained, except in the case of diabetic urine where very nearly the theoretical yield is obtained.

t = Temperature *in degrees Centigrade.*

T = Tension of aqueous vapour in millimetres of mercury at the observed temperature (t).

Example:—If 40 c.c. of nitrogen are evolved; and if the barometer at the time of the experiment stands at 29 inches; and if the temperature is 20° C.,

(*a.*) Convert inches of barometric reading to m.m.—*i.e.*, 29 × 25·399.

(*b.*) Then consult table of tensions of aqueous vapour (at Appendix A), and we see that at 20° C. the tension is 17·36.

$$\frac{40 \times (29 \times 25{\cdot}399 - 17{\cdot}36)}{760 \times (1 + 0{\cdot}003665 \times 20)}$$

$$= \frac{4 \times 736{\cdot}571 - 17{\cdot}36}{76 \times (1 + {\cdot}0733)}$$

$$= \frac{4 \times 719{\cdot}211}{76 \times 1{\cdot}0733}$$

$$= \frac{2876{\cdot}844}{81{\cdot}5708} = 35{\cdot}26 \text{ c.c.}$$

So that the 40 c.c. of nitrogen, when corrected for temperature, pressure and aqueous vapour's tension become 35·26 c.c.

If now the total amount of urine passed in the 24 *hours be known,* the total quantity of urea excreted per diem can be readily calculated.

Say that in a *non-diabetic* sample of urine the 5 c.c. of urine taken yielded 17·7 c.c. of nitrogen.

As 35·4 c.c. nitrogen = 0·1 gramme urea,
Then 17·7 c.c. = 0·05 grm. urea.

Then, if 5 c.c. urine yielded ·05 grm. of urea, how much urea would 100 c.c. of urine yield ?

$$\frac{100 \times \cdot 05}{5} = 10$$ per cent. (10 grms. urea in 100 c.c. of urine).

Now, supposing 2 litres (*i.e.*, 2000 c.c.) of urine have been passed during the 24 hours, this quantity would contain 10 × 20 = 200 grammes of urea.

If the sample is diabetic, substitute 37·2 for 35·4 in the above example and calculate exactly as above.

Note.—Urates and creatinin also yield up their nitrogen in this reaction but the error due to this may be neglected for clinical purposes.

DAILY AMOUNT OF UREA EXCRETED.—This varies a good deal, and is proportionate to the amount of nitrogen in the food.

The average amount of urea in a healthy adult man's urine is about ·30 to 40 grammes daily, or on an average about 2 per cent. It attains its normal maximum about 3 hours after a meal (especially if of proteids). Women excrete a smaller amount than men (on an average, 10 grains per stone of body-weight less). The ratio is as follows : 50 grains for each stone of body weight in a healthy adult man ; 5 per cent. less than this after 40 years of age ; and 10 per cent. after 50.

Diminution of the total amount of urea-output is a bad sign when occurring late in the course of Nephritis, of whatever form.* In Great Britain, too little attention appears to be given to the systematic estimation of urea in cases of nephritis. (On the other hand, " there is a danger abroad of allowing chemical circumstances too greatly to influence therapeutics.") Urea ought also to be estimated in Diabetes Mellitus, and particularly in cases in which uræmia or puerperal eclampsia may supervene.

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* When the urea is found diminished to less than half the average quantity it indicates pronounced renal inadequacy, and in surgical cases would contra-indicate a nephrectomy. *See also Cryoscopy.*

Urea is increased in amount by—Fevers, Diabetes Mellitus, and by Arsenic, Antimony, Phosphorus, Oxygen, Codeine or Morphine, or Ammonium salts, and by large doses of quinine. *Physiologically*, it is increased by large amounts of food (especially proteids), and some time after muscular exercise; by hot baths or cold applications to the skin, and by copious draughts of hot water.

It is decreased by a low diet; a vegetable or non-nitrogenous diet; when only small amounts of fluid are taken; by sedentary habits; by tea, coffee, alcohol; *small* doses of quinine; in certain forms of nephritis; in renal atrophy (primary or secondary); during the defervescent stage of fevers; in many liver diseases (notably acute yellow atrophy); in uræmia and diabetic coma; in most wasting or chronic diseases; and towards the end of most fatal diseases.

See also Cryoscopy.

PURIN BODIES (also called Alloxuric or Xanthin Bodies). This group of substances as found in the urine results from the decomposition of tissue-nuclein, or from ingestion of food containing xanthins and nucleins. Purin bodies contain purin (C_5H_4) as an essential part of their chemical structure.

Hypoxanthin, Xanthin, Adenin and Guanin are termed the Purin bases (Purin itself has never been detected in the body), and are mostly oxidised into uric acid while passing through the organism, and are also partly excreted as urea. In the urine the purin bodies chiefly present are xanthins, hypoxanthins and uric acid.

Boyd * states that the purin bases form generally $\frac{1}{10}$th the amount of uric acid present.

The urinary purins are classed as :—

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* Gibson & Russell's "Clinical Diagnosis," edited by F. D. Boyd, 3rd edition, p. 263.

Endogenous = derived from nuclein destruction in the tissues;
or *Exogenous* = directly derived from foods containing purin substances.

The Endogenous Purin Bodies (according to Hall and others) usually yield about ·16 grm. daily *of purin nitrogen* (or ·364 grm. uric acid, and ·095 grm. xanthin bases) *when the individual is on a purin-free diet.*

Their chief source is the nucleins of the body tissues. In the urine of very young children these substances are relatively greater in amount—due to more active metabolism. In diseases accompanied by leucocytosis the purins may be increased—both increases being expressions of the same pathological hyper-metabolism, in all probability. In order to determine the endogenous urinary purins the patient must be placed on a purin-free diet (milk, cheese, bread, sugar, butter, eggs, potatoes, and rice), and tea, cocoa, and coffee must be withheld during the experiments, as these contain tri- and dimethyl-xanthines (caffeine, theobromine).* It is at present doubtful what proportion of the endogenous purins are excreted as urea.

The Exogenous Purins are derived from purins ingested as food, of which about half is eliminated as uric acid and purins, and the rest as urea, or intermediate products between urea and uric acid. Purins in foods are "free" or "bound"—the "free" are excreted mainly as uric acid, probably within 12 hours, the "bound" within 48 hours. At present the relation which exists between urinary purins in health and disease has not been sufficiently ascertained, but when more precise information is forthcoming, it is expected that it will be possible to ascertain the rate of nuclein destruction occurring in the body, and also to regulate patients' diet according to their metabolic functions in a way that at present is impossible.

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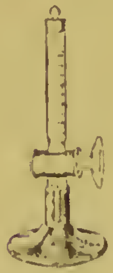
* Hall (*op. cit.* pp. 40–46) gives the following PERCENTAGE OF PURIN BODIES in the following foods :—

Fish.—Cod, ·0582; Plaice, ·0795; Halibut, ·1020; Salmon, ·1165. *Meats.*—Tripe, ·0572; Mutton, ·0965; Veal, ·1162; Pork (loin), ·1212 and (neck) ·0567; Ham, ·1155; Beef (ribs), ·1137; Sirloin, ·1305; Steak, ·2065; Liver, ·2752; Sweetbread, 1·0063; Chicken, ·1295; Turkey, ·1260; Rabbit, ·0970. *Vegetable foods.*—Oatmeal, ·0530; Peasemeal, ·0390; Beans (haricot), ·0637; Lentils, ·0637; Potatoes, ·0020; Onions, ·0090. *Beers.*—(1 litre), lager, ·0125; pale ale, ·0145; porter, ·0155. *Tea.*—Ceylon, ·0587; Indian, ·05; China, ·0365. *Coffee.*—·10.

The personal metabolic factor for the individual has been found to be constant for the same person under the same conditions.

Dr. Walker Hall, of Manchester, has devised a purinometer which allows of the ready approximate estimation of urinary purins. By this process the purins are pptd. by silver nitrate in ammoniacal solution. Hall's purinometer is a uniformly calibrated and graduated separator, with, at the foot, a well connected with the cylinder by a tap.


HALL'S PURINOMETER.

The following are Hall's directions for employing the instrument:—

(1.) The total daily mixed urine is freed from albumin. The purinometer's tap is closed and 90 c.c. of urine and 20 c.c. of solution A are poured into the instrument. A ppt. of phosphates results.

(2.) When this ppt. has fully separated out, open the tap and allow the ppt. to fall into the well. Allow on an average ten minutes for this, but do not wait more than 15 to 30 minutes.

(3.) Then close the tap and add solution B up to the 100 c.c. mark on the cylinder. There results a ppt. of silver chloride and silver purin. The former will dissolve gradually in the excess of ammonia present. Hasten this by slowly agitating the cylinder's contents. If any white flakes of silver chloride remain, add a few drops of strong ammonia solution to dissolve them.

(4.) Place the apparatus in a cupboard for an hour (preferably for 24 hours).

(5.) Then read off the amount of ppt. by the graduation on the cylinder.

(6.) Multiply the reading by 1·5 = percentage of purin bodies.

(7.) *To get the percentage of nitrogen present*, again multiply by ·001 (or whatever factor is given with the particular purinometer employed, as it varies for each instrument).

(8.) Then multiply by the daily amount of c.c. of urine = total daily purin nitrogen. The most accurate results are got when the sp. gr. of the urine is between 1015–25. If above or below this range, and if the ppt. is less than 10 c.c., multiply the number of c.c. read off by ·0015; if *over* 10 c.c. multiply by ·0012; if over 22 c.c. by ·001.

Solutions Required :—*

Sol. A.—*Ludwig's Magnesium Mixture.*
(Magnesium sulphate, 1 part;
Ammonium chloride, 2 parts;
Ammonia solution, 4 parts;
Distilled water, 8 parts;) 100 c.c.
Ammonia solution (20 per cent.), 100 c.c.
Talc (very finely divided), . 10 grammes.

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* Both solutions should be vigorously shaken before use.

Sol. B.—Silver nitrate, . . 1 gramme;
Strong ammonia solution, 100 c.c.;
Talc, ... 5 grammes;
Distilled water, . . 100 c.c.

Hall remarks that simple estimations of uric acid are "practically valueless," *except to indicate the onset or decline of an acute attack of gout or of leukæmia.* At the same time it is evident that *our present knowledge of the purin bodies is not sufficiently definite to enable any sufficiently exact generalisations available for clinical purposes to be made.* The method is given in order that any reader desirous of working at the subject clinically may have the *modus operandi* readily available. Further reference on the subject should be made to Walker Hall's "Purin Bodies," second edition, 1903, published by Shirratt & Hughes, London and Manchester.

Hall (*op. cit.*) summarises the existing observations as to the pathological increases and decreases of urinary purins thus:—

URINARY PURINS INCREASED—

Uric acid in alcoholism with enlarged liver; carbon monoxide poisoning; liver cirrhosis; gout; leucocythæmia; neurasthenia and migraine; pneumonia; sepsis; scurvy.

Xanthins increased in adiposity, diabetes (usually from excessive ingestion of meat purins), diphtheria, scarlatina, nephritis, "Thyroidea."

Uric acid decreased in anæmias and gout. Hall, however, points out that many of these observations are indecisive as the exogenous or food-derived purins were not excluded.

URIC ACID.

THE PIPERIDINE METHOD is the most convenient to employ clinically—much more so than Hopkins's process—and is sufficiently accurate for clinical purposes.

Piperidine is an organic base which unites readily with uric acid to form soluble salts. In the following process the uric acid is pptd. as ammonium urate by Ammonium Chloride. Then the uric acid is liberated from this compound by hydrochloric acid. The (piperidine) base is then run in until all the free uric acid is combined as piperidine urate, from which point the *alkaline* piperidine solution will redden the phenol-phthalein present. From the amount of base required for this the amount of uric acid is readily calculated.

This process has the great advantage over Hopkins's method of avoiding the use of Ammonium *Sulphate*—the solution of which filters very slowly.

Piperidine solution.—Dissolve 4·25 grms. of Piperidine in water and make up the bulk to 1000 c.c. Each c.c. contains 0·00425 grm. piperidine and corresponds to 0·0084 grm. of uric acid.

(1.) To 100 c.c. of urine (need not be albumin-free) add 30 grammes of solid ammonium chloride.* Allow to stand for two hours (preferably shaking the solution occasionally) in order that the ammonium urate may be completely separated.

(2.) Then transfer the ppt. to a filter and wash with ammonium *chloride* solution (30 grammes to 100 c.c. water).

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* The reagent must be quite free from ferrous salts.

(3.) Wash the urates off the filter with *boiling* water.*

(4.) Cool and add a few drops of hydrochloric acid to ppt. uric acid.

(5.) Filter off the uric acid and wash it with cold water until neutral to litmus paper (20 c.cs. of water generally suffice for this).

(6.) Now dissolve the uric acid in *boiling* water (not more than 30 c.c. are needed); and then add a few drops of phenol-phthalein solution.†

(7.) *While hot*, run in from a burette the piperidine solution until a distinct *pink colour* is produced —*i.e.*, which does not disappear on shaking. Then stop and read the burette.

(8.) Multiply the number of c.c. read off by 0·0084 = percentage of uric acid present.‡

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[*] Use a wash-bottle with a very small jet; and open out the filter-paper so that no ppt. is lost.

[†] *Phenol-phthalein solution:* 1 grm. of solid Phenol-phthalein in 100 c.c. of alcohol.

[‡] *Heintz's Method* is mentioned here as being one of the best known methods but it has been superseded by the other methods described and cannot be recommended for use. It is the simplest but the least reliable. The results are always too low as in it the uric acid never completely separates, therefore an addition is required to compensate for this, *see* (4). It requires a chemical balance and is therefore unsuited to clinical requirements.

(1.) Add 10 c.c. strong HCl to 100 c.c. of urine (*freed from albumin*), and stand for 24 hours in a cool place.

(2.) Then filter through a filter-paper of known weight, wash the crystals with equal parts of HCl and distilled water by means of a wash-bottle.

(3.) Dry the filter paper and uric acid crystals in a hot-air oven at 100° C.

(4.) Weigh. Subtract the already known weight of the filter-paper and the result is the percentage of uric acid. (To allow for the loss *above mentioned, add* 0·0038 *grm. uric acid* for each 100 c.c. urine taken for the test.)

In certain rare cases, however, uric acid cannot be separated in this way.

HOPKINS'S METHOD :—

Here uric acid and urates are pptd. by AmCl as Am urates (hence avoiding any risk of reduction), and estimated by titration with a solution of potassium permanganate. The uric acid is oxidised by the permanganate, which loses its colour thereby. When all the uric acid has been oxidised the permanganate's colour is no longer discharged. A modification which is shorter and less tedious than the regular process is here given.

(1.) Add—with brisk stirring—enough powdered *pure* (iron-free) AmCl to *saturate* 100 c.c. of the urine[*] which has been heated to about 50° C.[†] (30 grammes, or 1 oz., of AmCl generally suffices).

(2.) Then add 2 or 3 c.c. of strong ammonia solution.[‡]

(3.) Cover and stand—with occasional stirring—for two hours.

(4.) Then filter and wash out the vessel with 9 parts of Am *sulphate* (saturated solution) mixed with 1 part of water.[§] Wash the residue three or four times with the Am sulphate solution.[||]

This is the chief difficulty of the process as the filtration is very slow. The use of a suction-pump filter hastens the filtration.

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[*] Need not be albumin-free.

[†] The AmCl when passing into solution lowers the temperature of the fluid considerably; hence the advisability of heating the urine.

[‡] Neglect any ppt. of phosphates which may result.

[§] The Am sulphate used must be free from iron and from any trace of *chlorides* which would decolourise the permanganate solution.

[||] Where great accuracy is required it is advisable to measure the filtrate and to add to the final result ·001 grm. (of uric acid) for each 15 c.c. of filtrate. This addition is usually omitted in ordinary clinical estimations.

Example :—If 25 c.c. of filtrate were obtained, then $\cdot001 \times \frac{25}{15} = \cdot0017$ which is added to the burette-reading multiplied by ·00375.

(5.) Next wash the residue off the filter into a beaker with *boiling water* by means of a wash-bottle with a very small jet. Open out the paper so that no ppt. is lost, and use as little water as possible for the washing.

(6.) Now cool, and make up the bulk to 100 c.c. with distilled water.*

(7.) Add 20 c.c. of strong sulphuric acid.†

(8.) Then *at once* titrate with a $\frac{1}{20}$th normal solution of potassium permanganate (1·581 grammes to 1 litre of water). Keep shaking the flask while adding the permanganate solution. Go on until a GENERAL DIFFUSED *pink colour appears which lasts two or three seconds.*

(9.) Read off the amount of permanganate solution used.

Every c.c. = ·00375 grm. uric acid.

Multiply the burette-reading by this figure. Result = grms. of uric acid per 100 c.c. of urine.

Note.—(*a.*) Albumin does not interfere with the process.

(*b.*) Small amounts of phosphates may be neglected but if in large amount they should be pptd. by heat and filtered off before commencing the process.

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* Sodium carbonate is often added at this stage in order to dissolve up the ppt. This is unnecessary as the sulphuric acid does this effectually.

† The acid is added to dissolve up the urate ppt., to acidify, and also to raise the fluid's temperature to about 60° C. as the titration is best conducted with a warm solution.

(*c.*) If there is a *deposit of uric acid or urates*, be careful to thoroughly shake up the solution so as to mix well.

(*d.*) The presence of bile-pigments interferes with the titration by the permanganate solution.

Uric Acid.—In *normal* urine the uric acid is all combined as urates.

7–15 grains (about ·5 to 1 gramme) are on an average excreted daily. The amount is *increased* when nucleo-proteids or other purin-yielding substances are largely present in the diet, and when there is much nuclein-destruction occurring in the body—therefore (especially when the subject is not in training), after prolonged and severe bodily exercise, or if he has been leading a sedentary life; also by Turkish baths, and where such drugs as salicylic acid and its compounds, or pilocarpine (or any other drug which increases the number of leucocytes) are being administered. Also during, and directly after, a gouty paroxysm; in acute fevers, uric acid diathesis, pernicious anæmia, leucocythæmia, &c.; but the uric acid excretion is *diminished* before an attack of gout, by chlorosis, by administration of quinine, atropine, and alkalies, by strict milk diet, diabetes mellitus, chronic plumbism, chronic interstitial nephritis, and chronic diseases.

TOTAL NITROGEN should be estimated by Kjeldahl's process, which requires a properly equipped laboratory for its performance.

For adults the total nitrogen excreted in the urine is distributed as follows:—

Urea,	84–91	per cent.
Uric acid and purin bases,	1–3	,,
Creatinin,	about 3	,,
Ammonia,	2–5	,,
Indol, skatol, hippuric acid, pigments, and nucleo-albumin,	7–9	,,

The amount of urinary total nitrogen depends on the activity of metabolism of nitrogenous tissues, and on the nitrogen of the food. The amount is increased in diabetes mellitus and fevers, but is diminished in inflammations of the kidneys.

PHOSPHATES.

The Total Phosphates may most readily be estimated by the following process:—

(1.) Add 5 c.c. of sodium acetate solution (made by dissolving 50 grammes of the acetate in 450 c.c. of water, and then acidifying with 50 c.c. of glacial acetic acid) to 50 c.c. of urine.

(2.) Heat to about 80° C., and then run in a standard solution of uranium nitrate (17·7 grammes dissolved in 500 c.c. of water—1 c.c. being = ·005 grm. of phosphoric acid, P_2O_5).

(3.) When a drop of the urine so treated gives a *marked brown* colour when mixed with a drop of potassium ferrocyanide (*saturated solution*) the process is complete.

(4.) Read off the amount of uranium solution used, and calculate the percentage present of phosphates as phosphoric acid.

Example:—If 20 c.c. uranium solution were used, then 20 × ·005 = ·01 phosphoric acid in 50 c.c. of urine. Multiply by 2 to get the amount in 100 c.c. = ·01 × 2 = ·02 per cent. phosphoric acid present.

[The above process is sufficient, but the estimation of the phosphoric acid in combination with lime and magnesium is occasionally done instead. The process is much longer and more troublesome, and the above process gives the necessary information for clinical purposes equally well.]

Amount excreted daily.—From 2 to 4 grammes of phosphoric acid. About half this amount occurs as earthy phosphates.

CHLORIDES.*

After urea, they are the principal solids in normal urine. 10–16 grammes in 24 hours is the average quantity passed, but this varies with the amount taken as food.

They are *diminished*:—

(1.) In dropsical conditions generally.
(2.) There is a gradual diminution in acute fevers (especially pneumonia) until the crisis of the disease is reached.
(3.) During rest.
(4.) By cancerous and other cachexias.

THEY ARE INCREASED :—

(1.) By active exercise (bodily and mental).
(2.) Diabetes mellitus.
(3.) Recovery from acute fevers and dropsical conditions.
(4.) Hot and cold stages of ague, but *during the course* of no other fever.

---

* Chlorides are *detected* by adding a few drops of nitric acid to a small amount of urine in a test-tube and then adding some silver nitrate solution = white flocculent ppt. (This also consists partly of combinations of silver with uric acid, creatinin, &c.)

Chlorides cannot be *directly* estimated in urine owing to its colour which would generally interfere with the production of a sharp "end-reaction," and also because of the presence of organic substances which interfere with the test.

The following process gives rather too high results, as a rule, as purin bodies, &c., combine with the silver as well as the chlorides. The results obtained are sufficiently approximate for clinical purposes.

SUTTON-MOHR PROCESS:—

(1.) Place 5·9 c.c. of urine in a porcelain capsule and add one gramme of powdered pure ammonium nitrate.

(2.) Evaporate to dryness and then thoroughly char the residue by continued heating.

(3.) Dissolve the residue in *hot* water.

(4.) Neutralise with dilute acetic acid
[in order to remove any carbonates formed during (2)].

(5.) Then add a few grains of pure calcium carbonate followed by a few drops of neutral potassium chromate.

(6.) Then fill a burette with a deci-normal silver nitrate solution (made by dissolving 16·966 grammes of silver nitrate in a litre of water) and run this solution into the urine solution till a *permanent reddish-yellow colour* is obtained.

(At this point all chlorides have combined as silver chloride and from this point on the reddish-yellow silver chromate is formed if the addition of the silver nitrate solution be continued.)

Calculation :—

Each c.c. silver nitrate solution = ·0058 grammes of of sodium chloride.

The number of c.c. of silver nitrate solution used gives the number of parts of sodium chloride per 1000 parts of urine.

OXALATES.

There is no satisfactory method for estimating oxalates volumetrically, hence the necessity of describing a gravimetric method. The following is the most satisfactory process and will, no doubt, rapidly supplant Neubauer's process formerly so widely employed.

Autenreith's Process :—

1. To 500 c.c. of urine add excess of calcium chloride and ammonia solution until a strong alkaline reaction results. Then shake well.
2. Stand for 24 hours.
3. Filter.
4. Add 15 to 20 c.c. of 15 per cent. hydrochloric acid to the ppt.
5. Then add 150 c.c. of this solution (ether, 145 c.c.; absolute alcohol, 5 c.c.) and shake up. Repeat this four times.
6. Decant off the ether-alcohol extract, and allow to settle for an hour.
7. Filter through a *dry* filter-paper into a separator.
8. Now *distil* the alcohol-ether extract.
9. Evaporate the residue to about 5 c.c.
10. Alkalinise by adding calcium chloride and ammonia.

11. Then after half-an-hour treat with dilute acetic acid = ppt.
12. Allow to stand for 24 hours.
13. Collect ppt. on a hardened filter of known weight.
14. Incinerate in a previously-weighted capsule and weigh the residue of oxalates.
15. As 500 c.c. of urine were operated on, divide the result by 5 to obtain the percentage.

TOTAL SOLIDS.

Normally 50 grammes (about $1\frac{1}{2}$ ozs.) are passed daily.

Quantity is roughly obtained by multiplying by 2 the last two figures of the sp. gr. over 1000 and this gives the result in grammes per litre.

Example:—Sp. gr. is 1012. Then $12 \times 2 = 24$ grammes per 1 litre of the urine.

If this figure be now—(*a*) divided by 1000, and (*b*) multiplied by the number of c.c. of urine passed during the 24 hours it gives the total solids excreted during the 24 hours.

If the sp. gr. is over 1025, multiply the last two figures by 2·33 instead of by 2.

An estimate of the total solids is often recommended to be made by evaporating a given bulk to dryness in a weighed capsule placed on a water bath, then weighing until constant, and calculating in terms of grains or grammes passed in the 24 hours. This is very fallacious, as, during the drying to constant weight, urea is freely decomposed.

Calculate from the sp. gr. as above described.

TOTAL ACIDITY.

Acidity is chiefly due to di-hydrogen sodium phosphate, and other acid salts.

This may most easily be estimated in terms of oxalic acid,* but no method proves quite satisfactory in the case of urine.

1. Make a deci-normal soda solution by dissolving 4 grammes of stick caustic soda in 100 c.c. of water.

(As this amount would exactly neutralise 6·3 grms. of oxalic acid, so 1 *c.c. of this solution neutralises* ·0063 *grammes of oxalic acid.*)

2. Pour this solution into a burette.
3. Then place 50 c.c. of the urine in a flask and add the caustic soda solution till a drop of the solution produces a red colour when placed on blue litmus paper, and a blue colour when placed on red litmus paper.†
4. Read off the amount of soda solution used, and multiply the number of c.c. by ·0063 = amount

---

* (Were it desired to express the acidity in terms of phosphoric acid in view of the urine's acidity being normally mainly caused by di-hydrogen sodium phosphate, it would be necessary to calculate the amount of phosphoric acid combined as this phosphate as compared with the total amount present of phosphoric acid. This is lengthier and the results hardly justify the preference of this method over the estimation in terms of oxalic acid which will, therefore, be alone given here.)

† Violet paper may be used instead as being more sensitive. Read off the amount of soda when no change of colour is produced by placing a drop on the violet paper. Cochineal solution is another excellent indicator to employ when making the above estimation.

of acidity in 50 c.c. of urine. Then multiply by 2 = *acidity percentage.*

The estimation of the acidity is very rarely required—*e.g.*, in diabetes mellitus, acid dyspepsia, fevers, gout, &c.

UROBILIN.—This pigment is markedly increased in pernicious anæmia, malarial fever, and certain other pathological states, and a quantitative estimation of it may be made by the following process (Garrod's) :—

(1.) Saturate a portion of the twenty-four hours' collected urine with ammonium sulphate. This ppts. urates and any uric acid present.

(2.) Filter off this ppt.

(3.) Then acidify the filtrate with dilute sulphuric acid.

(4.) Again saturate with ammonium sulphate = ppt. of urobilin.

(5.) Filter and collect the residue on the filter.

(6.) Dissolve the residue in water.

(7.) Again saturate this solution with ammonium sulphate (in order to further purify the urobilin by re-pptn.).

(8.) Collect the ppt. of urobilin, and dry.

(9.) Weigh.

Normally, urobilin exists in very small amount in the urine, mostly as a colourless chromogen.*

Urobilin gives a *green fluorescence* if dissolved in alcohol, and this appearance becomes much more pronounced when ammonia and zinc chloride are added to the solution.

TOTAL ALKALINITY.

This estimation is rarely if ever required for clinical purposes. The methods ordinarily recommended are titration with deci-normal solutions of oxalic, hydrochloric, or sulphuric acids.

SULPHATES generally vary directly as the amount of urea present. They may be estimated volumetrically or gravimetrically, but as such estimations are practically unheard of *for clinical purposes*, and as the processes require to be carried out in a well-equipped laboratory, I propose to omit a description of them, as also of those for estimating carbon dioxide, potassium, sodium, ammonia, calcium, magnesium, hippuric acid, creatinin, and fat. The estimation of such substances is, from a clinical point of view, merely of academic interest and is practically never needed in clinical urine examination.

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* Urobilin further gives, when examined by the spectroscope, a characteristic appearance. (*See figure.*) It is identical with stercobilin, the pigment of the fæces. Urochrome, the normal pigment of urine, is probably oxidised urobilin.

NOTE ON THE DISCRIMINATION OF URINARY CALCULI.

Urinary Calculi are merely agglomerated sediments.

IN ACID URINE—

Uric acid nucleus on which oxalate of lime is concentrically deposited (and, rarely, Cystin).

IN NEUTRAL URINE—

Crystalline calcium phosphate or carbonate.

IN ALKALINE URINE—

(*a.*) Amorphous calcium phosphate;
(*b.*) Triple phosphate; or
(*c.*) Acid ammonium urate.

More commonly calculi contain two or more ingredients though not infrequently calculi composed of a single ingredient are encountered.

When formed by a conglomeration of urinary deposits they are termed *primarily formed.*

When formed round some foreign body (*e.g.*—a broken catheter-end in the bladder), they are said to be *secondarily formed.*

The three principal varieties of calculi are—

I. Uric Acid and Urates.

(reddish, smooth or tuberculated).

II. Phosphatic.
- (*a.*) Calcium phosphate;
- (*b.*) Ammonio-Magnesian phosphate;
- (*c.*) Calcium and magnesium phosphates.

(white and relatively soft).

III. Oxalate of Lime ("Mulberry").

(brown or grey, mulberry-shaped or smooth—when smooth called "hemp-seed calculi.")

Xanthin and cystin calculi are rare.

Calcium carbonate occurs (along with Calcium phosphate) frequently in prostatic calculi which may also contain traces of uric acid, triple phosphate and calcium oxalate. Fibrinous and "uro-stealithic" (fatty) calculi are very rarely encountered.

Mode of Examination—

Cut the calculus in half and scrape a little from each of the different layers of which it may be composed.

I. HEAT OVER A SPIRIT LAMP ON A PLATINUM OR MICA FOIL = IT COMPLETELY MELTS AWAY.

It may be—
- (*a.*) Uric acid;
- (*b.*) Urates;
- (*c.*) Cystin; or
- (*d.*) Xanthin.

(*a.*) *Take some more of the powder, add a little water, stir, and then* Heat.

= it dissolves (urates; cystin; xanthin);

= if it does *not* dissolve, proceed to test for oxalates, phosphates, and carbonates (see II.).

(*b.*) *On cooling, the urates separate out and render the fluid turbid.* Examine under microscope for urate granules or crystals and for cystin.

(*c.*) *Xanthin gives the Xanthin reaction—i.e.*, evaporate with nitric acid and touch residue with caustic alkali = red. Heat = becomes reddish-violet. (*See* also p. 47.)

II. IF A RESIDUE IS LEFT ON THE FOIL.

(*a.*) *Treat some of the powder with hydrochloric acid and heat.*

= soluble with effervescence (CARBONATE—generally of calcium);

= it quietly dissolves (PHOSPHATE OR OXALATE).

Then add Am. = ppt. of both or either.

Add acetic acid = dissolves (*phosphates*);

= does not dissolve (*oxalates*).

Examine microscopically for crystals of above.

If an *insol.* residue is left after treatment with HCl examine for URIC ACID by the murexide test (page 42).

(*b.*) *Add ammonia solution to the solution:—*

IF THE RESIDUE DISSOLVES = *CYSTIN.*

Evaporate the solution and examine microscopically for cystin; or

XANTHIN = gives xanthin reaction (*see above*).

(*c.*) *If the powder melts, giving off ammoniacal fumes but leaving a residue* = CALCIUM PHOSPHATE; OR MAGNESIUM PYROPHOSPHATE (generally known as "fusible calculus").

CRYOSCOPY.

THIS is a means of obtaining from the FREEZING-POINT OF THE BLOOD AND URINE an indication of the excretory activity of the kidneys. The method is based on an indisputably sound theoretical basis and its practical indications have given results of great value especially in cases of doubt as to whether or not a patient should be subjected to a severe surgical operation. The question of renal adequacy is one which * is in most cases answerable from the indications given by this method.

In chronic forms of *nephritis*, and especially in interstitial nephritis, this method gives valuable indications of the lessened excretory power of the kidneys and acts in many cases as a danger-signal.†

The eliminating power of the kidneys has also been tested by administration of either methylene blue or phloridzin, and these methods will be referred to later.

The determination of the freezing-point of both blood and urine can be made very simply. The information so obtained can be got in no other way known at present.

---

* Especially so in helping the surgeon to decide between a nephrotomy or a nephrectomy.

† In cardiac disease and in certain functional circulatory diseases in which the kidneys' functions are being badly performed, the method should also give useful indications.

The process is based on the fact that the greater the number of molecules in solution the lower is the freezing-point. That is to say that the freezing-point shows the degree of *molecular concentration* (or, as it is termed, " osmotic pressure ") in the fluid while the specific gravity* shows the weight of solids in solution in it.

In *simple* solutions, estimations of the freezing-point give very similar results, but in complex fluids like blood or urine there is much difference in the results obtained. For example, IN BLOOD *the freezing-point normally varies only from ·55 to ·57° C. below that of distilled water*, while the specific gravity varies from 1046–1057.

Again IN URINE *the freezing-point normally varies from 2 to 0·9° C. below the freezing-point of distilled water;* and the freezing-point and specific gravity further vary markedly at different periods during the twenty-four hours.

Koranyi † and Kümmel ‡ have been the pioneers of the method in its practical application to clinical work, and the following facts have been amply proved, viz. :—

(1.) So long as even one of the kidneys is healthy the blood's freezing-point never falls below $-0·56°$ C.

(2.) Renal inadequacy results in a marked increase in the blood's molecular concentration, and the freezing-point falls below $-0·56$ [The lowering of the freezing-point may be also effected by deficient oxidation, as in cachexias and chlorosis: administration of oxygen removes this in such a case but has no effect in the case of renal inadequacy.]

---

* If the *decimal portion of the* sp. gr. figure of NORMAL urines at 15° C. be multiplied by the factor 75, the freezing-point of the urine may be approximately obtained.

† Zeitschr. f. Klin. med., vol. 34.

‡ Verhandl. deut. Gesell. f. Chir., vols. 29, 30, 31.

(3.) One-sided renal disease does not necessarily lead to renal inadequacy, as the increase in activity of the sound kidney may compensate for the defective excretion of the diseased kidney.* But when the *blood's* freezing-point shows a variation from normal, it points to disturbance of the renal functions—*e.g.*, if the blood-freezing-point is found to be −·65 or −·68 it would clearly point to inadequate excretion by both kidneys.

---

* A diseased kidney, however, occasionally exercises a deleterious effect on the excretory power of the other healthy kidney.

METHOD.

The Apparatus consists of:—

(*a.*) Glass tube in which the urine or blood is placed (this tube is 1 inch in diameter and 4 inches long).

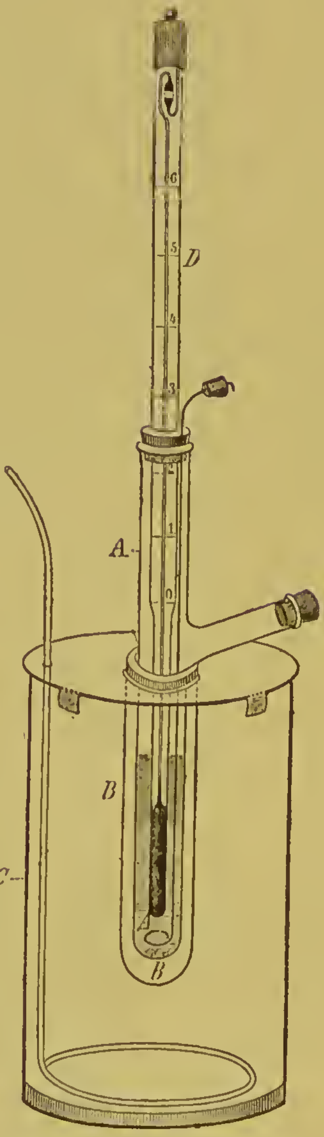
(*b.*) A second tube into which (*a*) is placed, and which acts as an air-chamber.

(*c.*) Both these tubes fit into a glass cylinder, which contains the freezing mixture (ice and salt. See Appendix B.).

(*d.*) A thermometer graduated in $\frac{1}{100}$ths.° from $-5°$ to $+1°$ C.

(*e.*) A platinum or copper ring-stirrer.

Both (*d*) and (*e*) are fitted into (*a*).



Friedenthal's Freezing Apparatus.*

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* The apparatus costs £1, 5s. It is a modified Beckmann's apparatus.

MODE OF PROCEDURE.

Both blood and urine should (especially in surgical cases) be separately examined, as the blood's freezing-point only tells us of the general adequacy of renal excretion, whereas the freezing-point of urine obtained from each ureter indicates which kidney is functionally inadequate.

(1.) *Blood.*—From 2 to 4 drachms of blood are removed from a vein by venesection, or through a sterilised hollow needle, and at once placed in tube (*a*), and then plunged *in the freezing mixture.*

Urine.—Place from 2 to 4 drachms of *freshly voided* urine * in tube (*a*), and plunge *in the freezing mixture.*

(2.) Place the thermometer in the fluid in (*a*), so that the entire bulb is covered.

(3.) Then insert the metal stirrer so that its end lies below the thermometer-bulb.

(4.) When the thermometer's mercury has left the reservoir-bulb, remove (*a*), and place it in the air-chamber (*b*), which latter is now plunged in the freezing mixture.

(5.) Keep stirring until the process is completed, so as to keep the blood equally cooled. When freezing is about to occur, stir more vigourously.†

(6.) The thermometer first falls perhaps to – 2° or – 3° and then rapidly rises to the maximum freezing-point where it remains for some time. Read this = freezing-point.

---

* The urine need not be freed from albumin.

† The stirrer works vertically.

This point in cases of renal adequacy is found to be, for blood, – 0·56° C. below the freezing-point of distilled water. *It may normally vary* $\frac{1}{100}$th° *above or below this figure.* If greater variations are found = imperfect elimination of solids by the kidneys. If the freezing-point is lower than – 0·58 in a case requiring a surgical operation, postpone the operation until the freezing-point is somewhere between – 0·57° and – 0·55°.

If the blood's freezing-point is – 0·56 one kidney must be sound, and, as one healthy kidney suffices to carry on the renal excretory work, surgical interference with the diseased kidney may (*cæteris paribus*) be proceeded with.

If the blood's freezing-point is – 0·59, nephrectomy would only be admissible after ascertaining:

(*a.*) The freezing-point of the urine obtained from each ureter separately; and,

(*b.*) The amounts of urea and (by phloridzin injection) of sugar.*

If the blood's freezing-point is – 0·60, nephrectomy is inadmissible (except where an abdominal tumour is present as when this is the case the freezing-point may be lowered without the existence of renal inadequacy).† In many cases in which the blood's freezing-point was found to be much below normal, nephrotomy has been performed and the freezing-point has subsequently risen enough to justify nephrectomy which has repeatedly been successfully performed in such cases.

---

* Of course this applies to cases in which glycosuria does not already exist. The estimation of urea and sugar are made as ordinarily.

† Kümmell advises the surgeon in such cases when considering the question of nephrectomy to trust to the ordinary urinary tests and the phloridzin method (*which see*) rather than to cryoscopy.

The urine's freezing-point normally varies from 0·9° to 2·0°C. below the freezing-point of water, as has already been pointed out, but if it is below this it indicates defective excretory power. Compare the freezing-point of the urine separately drawn off from each ureter.*

G. H. A. Clowes † has worked at an application of Cryoscopy combined with observations of the sp. gr. of the urine for the estimation (approximately) of sugar in urine, and has also applied somewhat the same principle to the estimation of albumin. These methods need not be detailed here as the results require confirmation by other workers, but the reference is given for the use of anyone interested in the subject.

DRUG-TESTS OF RENAL EXCRETORY POWER.

Methylene Blue and Phloridzin ‡ have both been largely employed for testing this. They have the advantage over urea-estimations that a known amount of the substance is administered, and the degree of retardation or prolongation of the elimination can thus be judged. The comparative excretory power of the kidneys can be gauged in this way by ureteral collection of the urine from each kidney.

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* *Catheterisation of the ureters.*—There is always a risk of infecting a healthy kidney from the bladder by catheterising its ureter. In order to avoid the risk attending ureter-catheterisation, Luys's (of Paris) instrument may be employed. [*See* "La Séparation de l'urine des deux reins," by Dr. Luys (Gazette hebdom. de Médic. et de chir., 11th December, 1902)]. A specially devised double catheter is passed into the bladder. The bend at the end of this instrument is pressed down on the floor of the bladder and then in this bend a diaphragm is raised so that each ureter discharges into a corresponding depression on the bladder-floor from which the urine is drawn off separately through the double catheter.

† *American Journal of Physiology*, vol. ix., No. v., 1903.

‡ Phloridzin causes a temporary glycosuria. The sugar is estimated by the ordinary methods.

Methylene Blue Method.

I. One gramme of chemically pure methylene blue is dissolved in 20 c.c. of distilled water.
II. Filter of any ppt. or suspended particles.
III. Boil in order to sterilise.
IV. Then inject, with antiseptic precautions, 1 c.c. of this solution into the gluteus maximus—the patient having been directed to empty the bladder immediately before the injection.
V. Collect the urine at intervals of half-an-hour, 2, 3, 6, 12, or 24 hours, and note the result.

Methylene blue is first of all excreted as a colourless chromogen ; so, in order to detect it in urine, add a few drops of acetic acid and heat the urine = green or blue colour.

Later on—generally within half-an-hour in normal cases—the urine is pale green. This deepens later until 3 or 4 hours after administration of the drug the urine has attained its maximum depth of colouration—a dark green. This colour persists in the urine passed for the next few hours, and then gradually fades. 40 to 50 hours after administration the drug has quite ceased to colour the urine, in normal cases.

PATHOLOGICALLY, we may find—

(1.) Delay in appearance of the colourless chromogen.

(2.) The appearance of a green or blue colour may be delayed, but the colourless chromogen is excreted as in a normal case.

(3.) The blue colour may intermit and may not follow the usual course already described.

(4.) The period of excretion of the drug may be much prolonged.

PHLORIDZIN-METHOD.

I. Test for glucose in the ordinary way.*

II. The patient empties the bladder just before the injection is given.

III. Inject (antiseptically) 1 c.c. of phloridzin (a 1°/。 solution made by dissolving the phloridzin in water by the aid of sodium carbonate).

IV. Collect the urine every half-hour, and estimate the sugar by Fehling's or Pavy's method.

The elimination of sugar should last from two to four hours and 1–2 grms. of glucose are usually excreted (but this may vary from ½ to 2½ grms. normally).

Pathologically we may have the variations in excretion as in the case of methylene blue—*i.e.*, delay in the appearance of sugar, intermittence, or prolongation of the period of excretion.

In acute and subacute (parenchymatous) *nephritis*, glucose is not excreted although methylene blue is.

In interstitial nephritis (even when there is no albuminuria), the excretion of both methylene blue and of sugar is diminished; or the appearance of the chromogen or sugar is delayed; or the excretion period may be prolonged.*

---

* If glycosuria is present, employ the Methylene Blue method instead.

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* Achard and Castaigne: Monographies Cliniques, No. 23, 1900: Masson & Co., Paris.

ILLUSTRATIONS OF URINARY DEPOSITS.

These illustrations have been drawn mainly from microscopic preparations made by the Author, except in the case of those whose source is indicated in the Preface or on the plates, and those illustrating Filariæ, Distoma or Bilharzia hæmatobium, and Gonococci, which have been reproduced by permission of the Author and Publishers (and in a modified form) from Scott's "Clinical Examination of the Urine" (J. & A. Churchill).

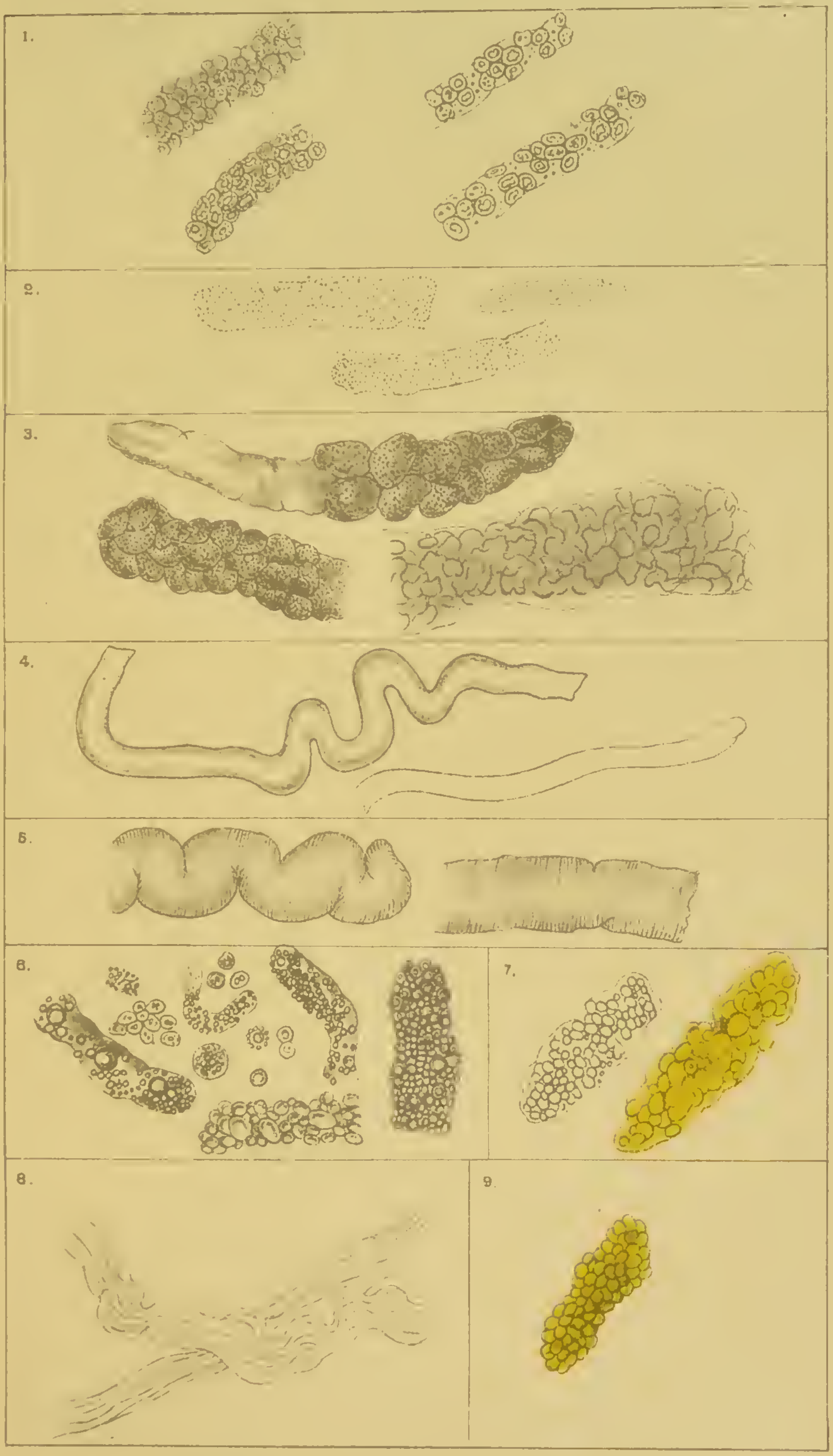
The specimens have mostly been drawn when placed under a high power of the microscope (300 *to* 500 *diameters*). *Specimens drawn with powers* less than 300 *diameters are so indicated.*

INDEX TO ILLUSTRATIONS.

Plate I. Casts.
,, II. Epithelium, Blood, Pus, Fat.
,, III. Gonococci, Tubercle Bacilli, Spermatozoa, Hippuric Acid, Cholesterin.
,, IV. Osazones, Leucin, Tyrosin.
,, V. Bilharzia, Filariæ, Cystin.
,, VI. Oxalates.
,, VII. Uric Acid, Sodium or Ammonium Urate.
,, VIII. Urates (Ca, Am, Na), Urea Nitrate.
,, IX. Phosphates.
,, X. Spectra of Blood, Hæmatoporphyrin, Urobilin, &c.

PLATE I.

CASTS.



1.—Pus or Leucocyte Casts.

2.—Granular Casts.

3.—Epithelial Casts. *(After Ultzmann.)*

4.—Hyaline Casts.

5.—Colloid (waxy) Casts.

6.—Fatty Casts.

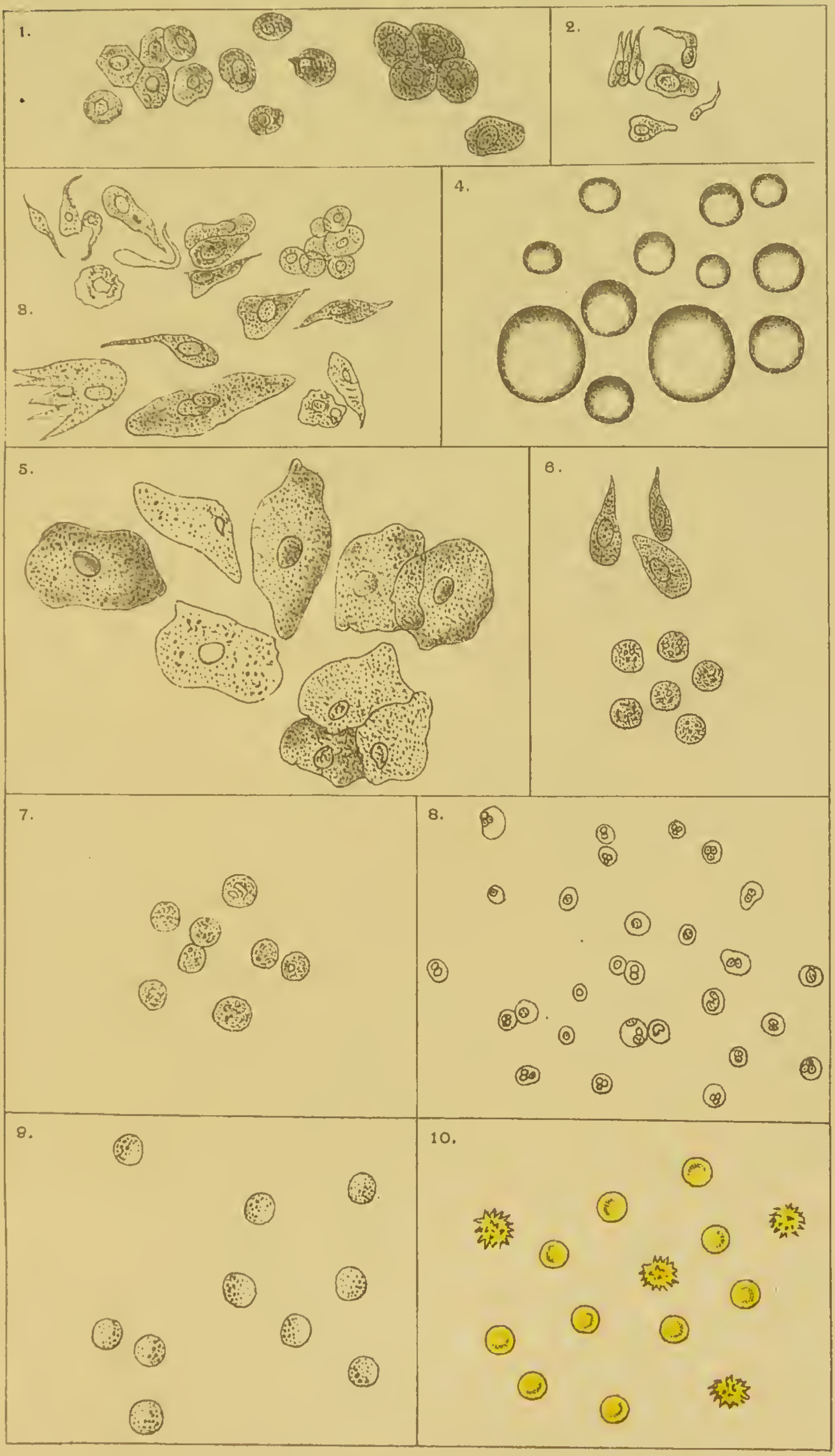
7.—Blood Casts.

8.—Mucous Casts.

9.—Ammonium Urate Cast.

PLATE II.

EPITHELIUM, PUS, BLOOD, &c.



1.—Renal Epithelium.

2.—Ureter Epithelium.

3.—Bladder Epithelium.

4.—Fat Globules.

5.—Squames (vaginal, vesical, preputial).

6.—Urethral Epithelium.

Pus Cells (showing nuclei).

7.—Pus Cells (leucocytes).

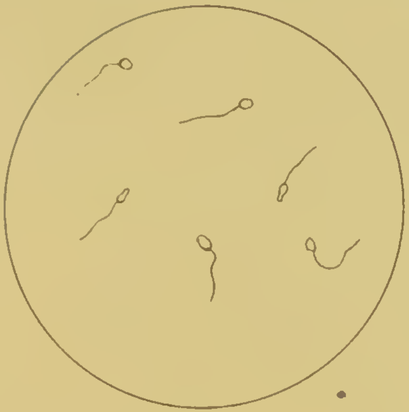
8.—Pus Cells (cleared with acetic acid).

9.—Swollen Pus Cells.

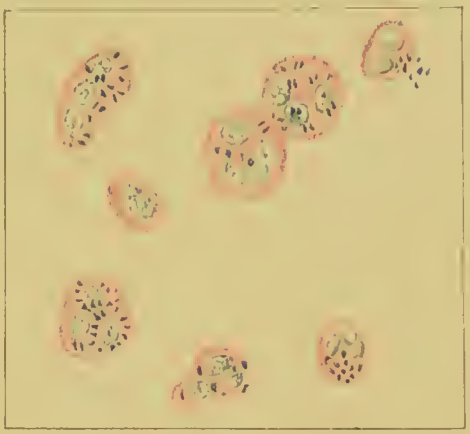
10.—Red Blood Cells (showing four crenated corpuscles).

PLATE III.

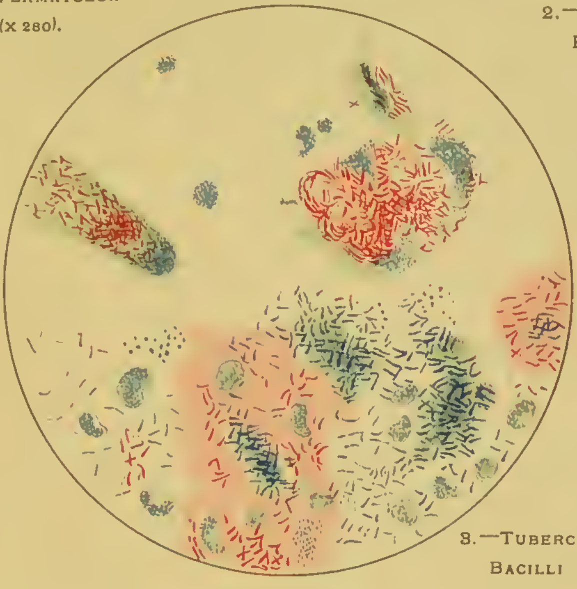
MICRO-ORGANISMS, &c.



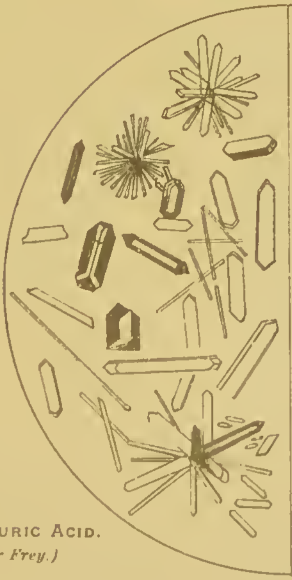
1.—Spermatozoa
(x 280).



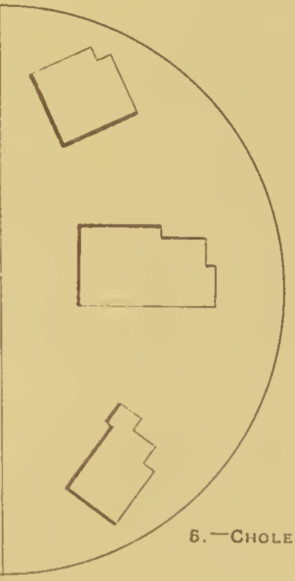
2.—Gonococci in
Pus Cells.



3.—Tubercle
Bacilli
(stained red.)



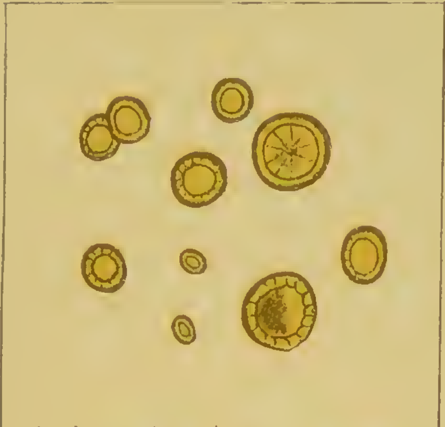
4.—Hippuric Acid.
(After Frey.)



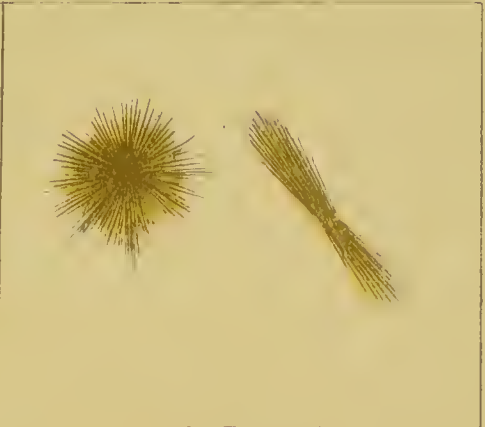
5.—Cholesterin.

PLATE IV.

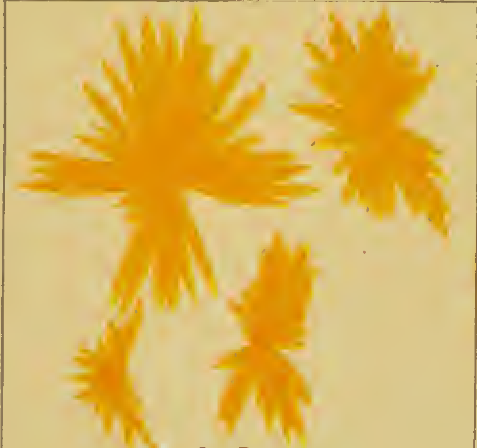
OSAZONES, LEUCIN, &c.



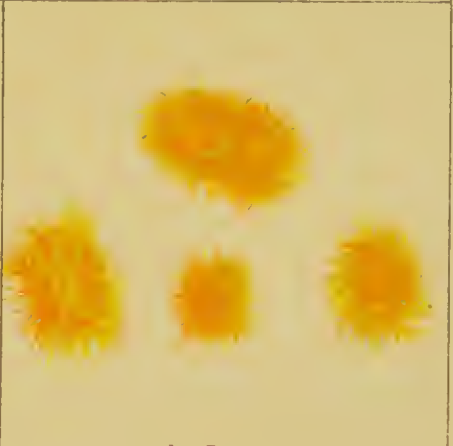
1.—Leucin (balls).



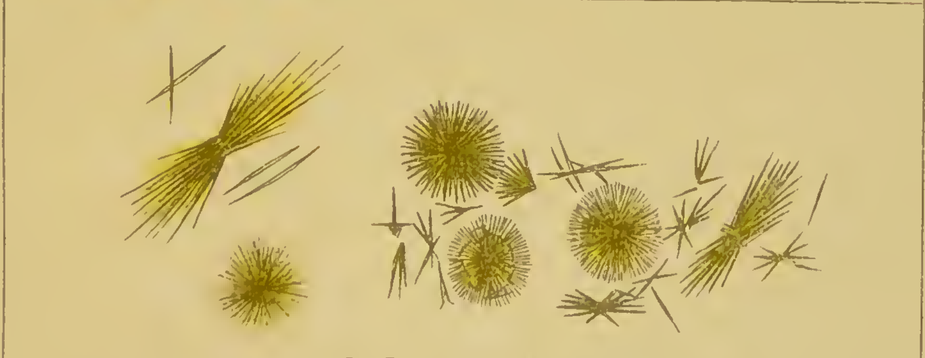
2.—Tyrosin (star, sheaf).



3.—Phenyl-maltosazone.

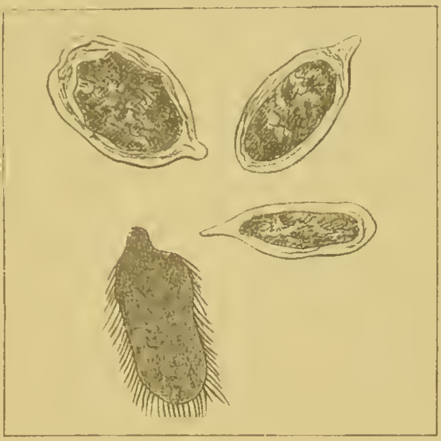


4.—Phenyl-lactosazone.

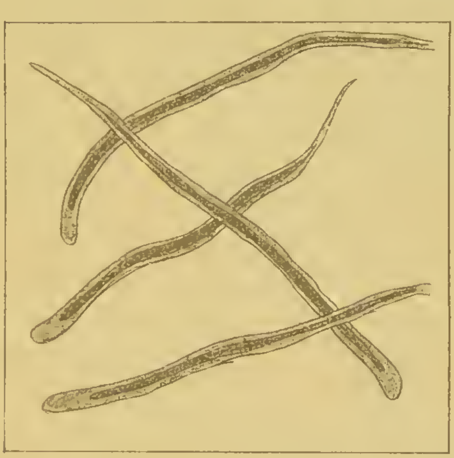


5.—Phenyl-glucosazone.

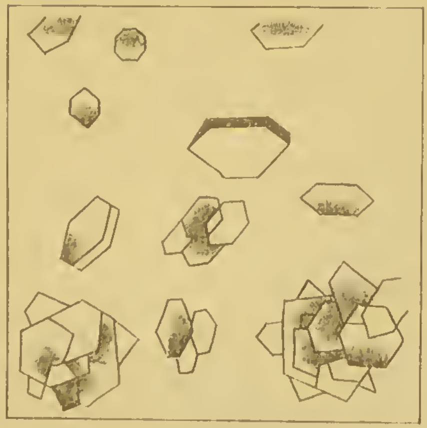
PARASITES, CYSTIN.



1.—Ova and Embryo
of Bilharzia
Hæmatobium.



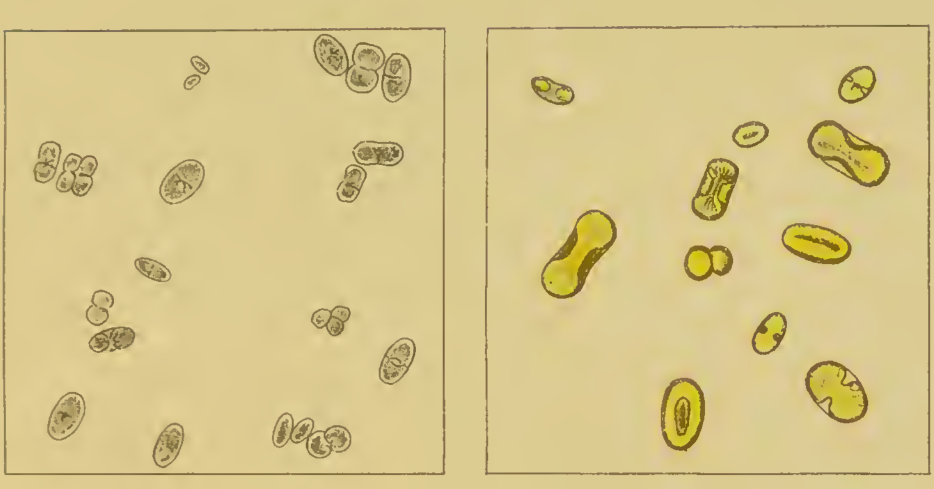
2.—Embryos of Filaria
Sanguinis
Hominis.



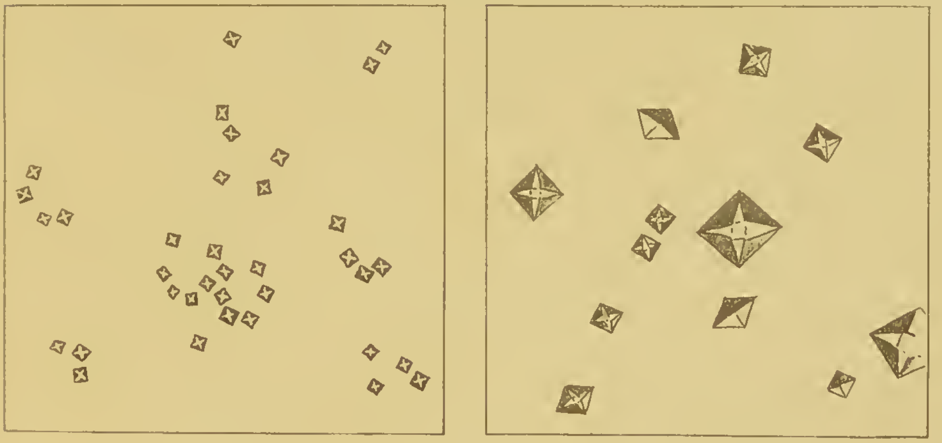
8. —Cystin.

PLATE VI.

CALCIUM OXALATE.



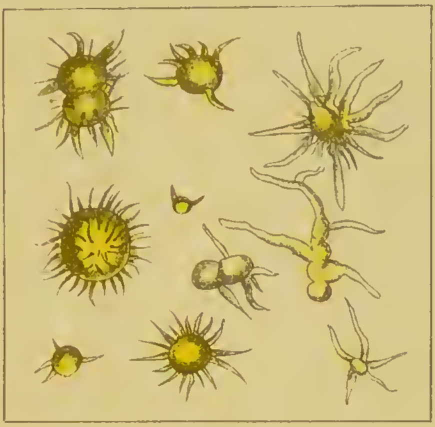
1.—Dumb-Bell Form (x 280).



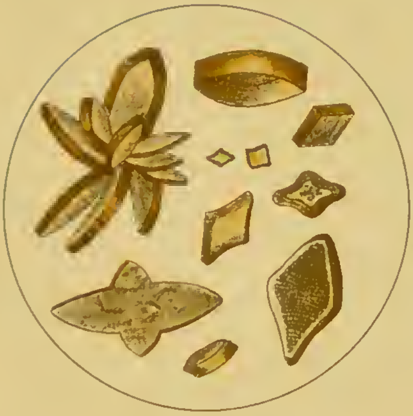
2.—Octahedra (various sizes)
(x 280).

PLATE VII.

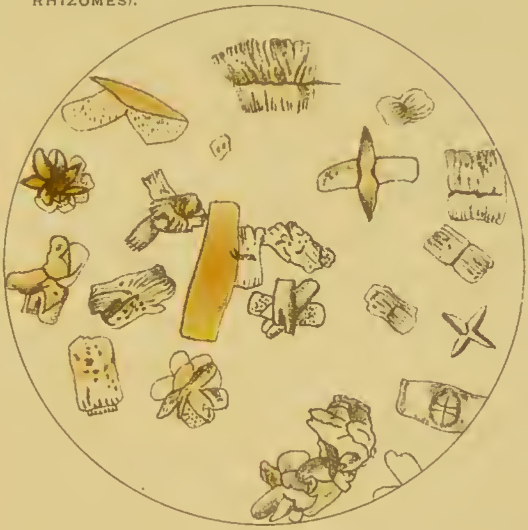
URIC ACID AND URATES.



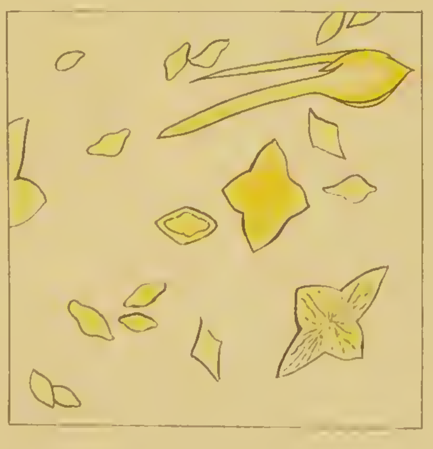
1.—Sodium or Ammonium Urate (spiculated globules and rhizomes).



2.—Uric Acid (star, cross, lozenge, cube forms).



3.—Uric Acid (various forms) (x 95).

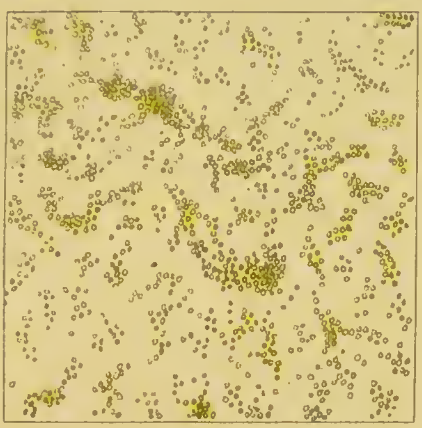


CLUB-SHAPED FORM.

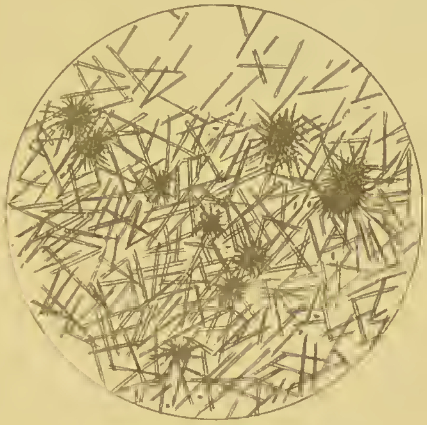
4.—Uric Acid (crosses, lozenges, whetstones).

PLATE VIII

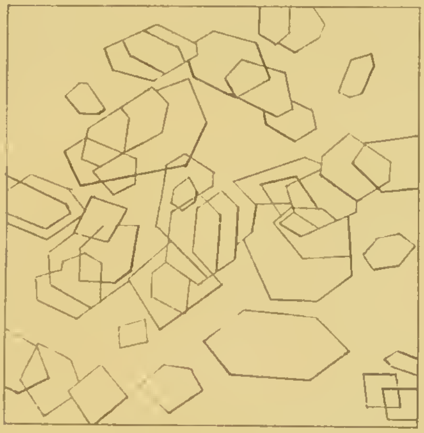
URATES, &c.



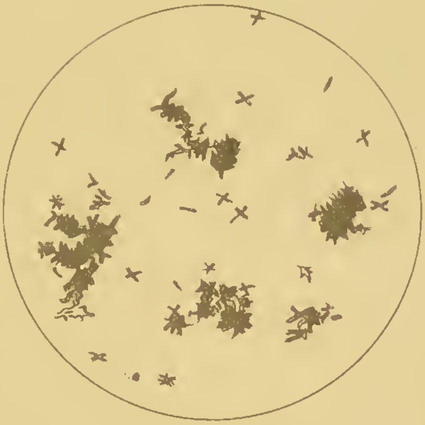
1.—Amorphous Urates.



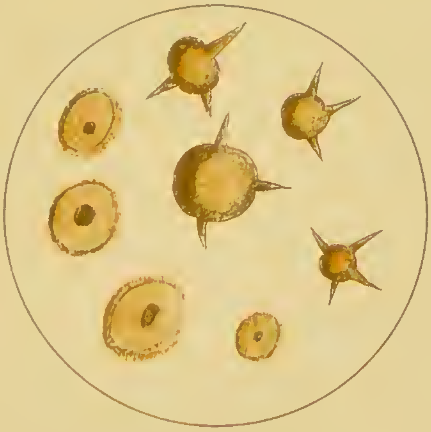
2.—Calcium Urate
(x 280).



3.—Urea Nitrate.

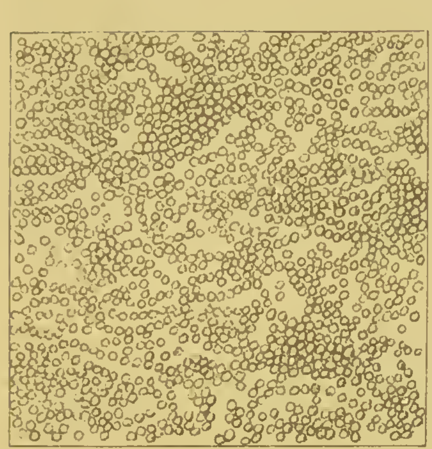


4.—Ammonium Urate
(x 280).

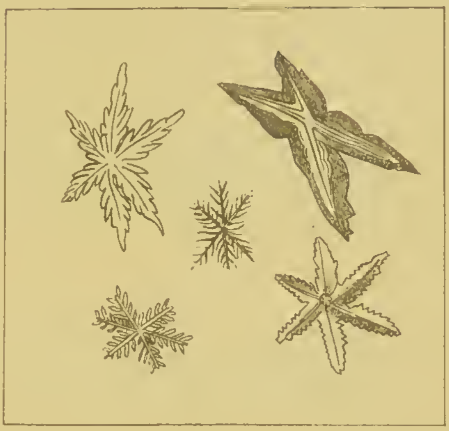


5.—Acid Sodium Urate.

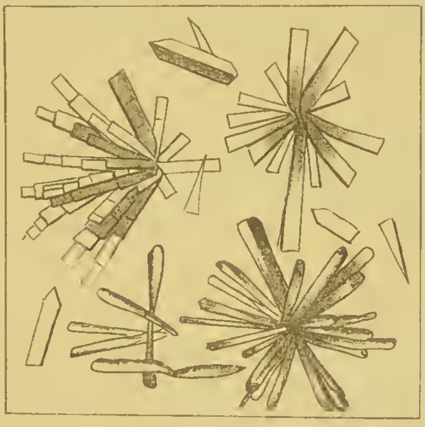
PHOSPHATES.



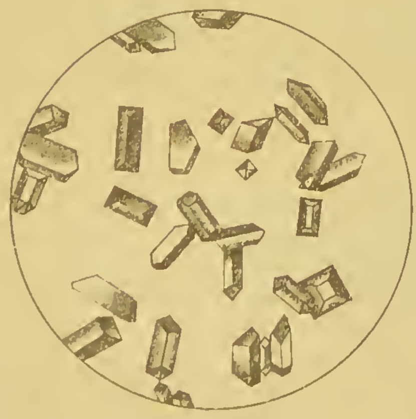
1.—AMORPHOUS.



2.—TRIPLE (FEATHERY, SHEARS-LIKE, STAR-FISH, AND FERN-LEAF FORMS).



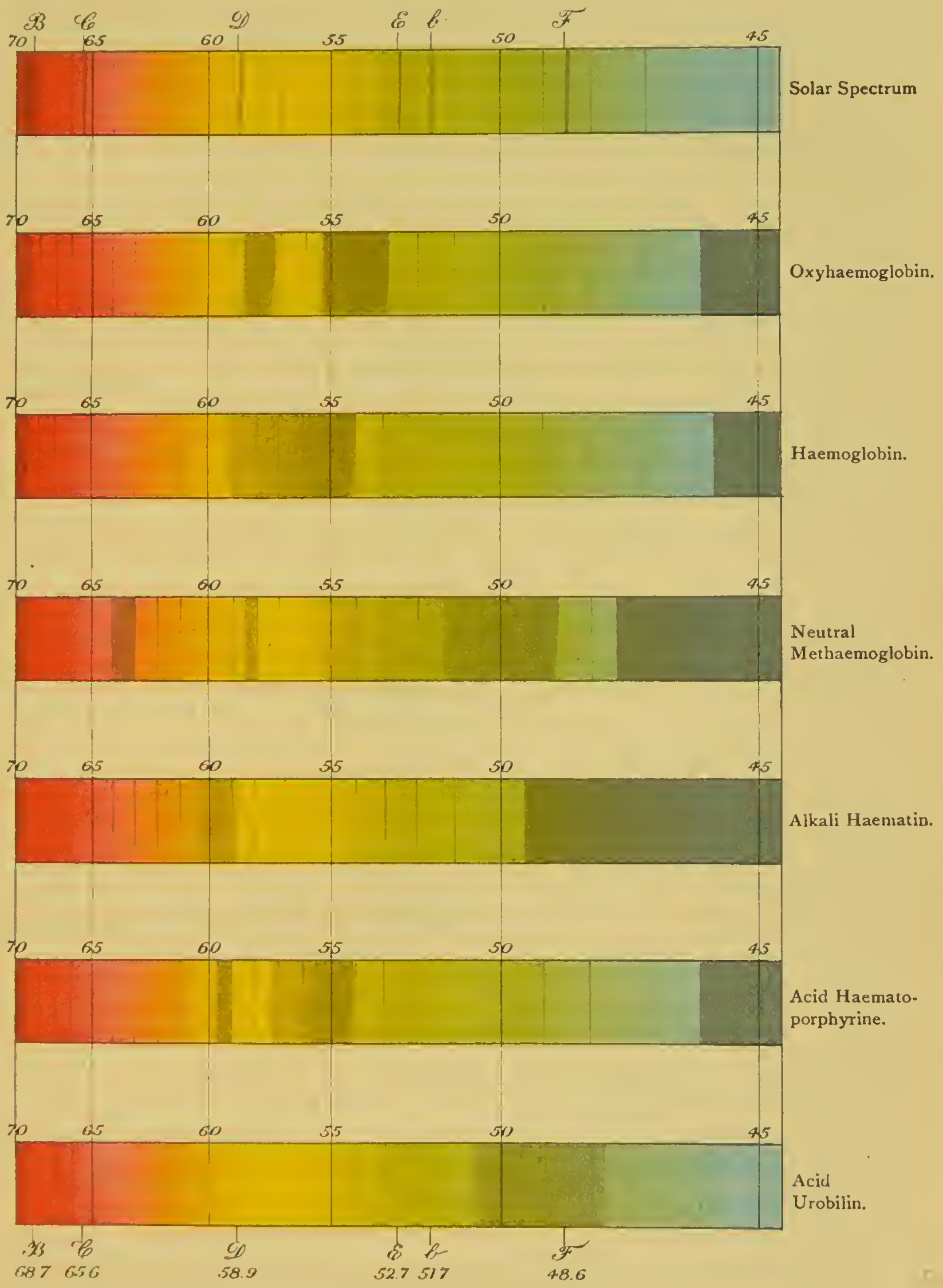
3.—STELLAR.



4.—TRIPLE (KNIFE-REST FORM) (X 280).

PLATE X.

SPECTRA OF BLOOD, HAEMATOPORPHYRINE, UROBILIN, &c.



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APPENDICES.

APPENDIX A.

Table of Tensions of Aqueous Vapour in millimetres of Mercury, from 10° to 45° C., reduced to 0° C. and the pressure at sea-level.

10°— 9·14
11 — 9·77
12 —10·43
13 —11·14
14 —11·88
15 —12·67
16 —13·51
17 —14·40
18 —15·33
19°—16·32
20 —17·36
21 —18·17
22 —19·63
23 —20·86
24 —22·15
25 —23·52
26 —24·96
27 —26·47
28°—28·07
29 —29·74
30 —31·51
31 —33·37
32 —35·32
33 —37·37
34 —39·52
35 —41·78
36 —44·16
37°—46·65
38 —49·26
39 —52·00
40 —54·87
41 —57·87
42 —61·02
43 —64·31
44 —67·76
45 —71·36

APPENDIX B.

1 minim	=	0·05916	cubic centimetre.
1 fluid drachm	=	3·5495	,,
1 ,, oz.	=	28·396	,,
1 ,, pint	=	567·92	,,
1 ,, gallon	=	4545·96	,,

1 cubic centimetre	=	16·63	minims.
1 litre (1000 c.c.)	=	35·21	fluid ounces.
1 grain	=	·064	gramme.
1 ounce (avoirdupois)	=	437·5	grains = 28·35 grammes.

To convert :—

Grammes per 100 c.c. into *grains per gallon*, multiply by 700.

,, ,, 100 c.c. to grains per fluid ounce, multiply by 4·375.

,, ,, litre to grains per gallon, multiply by 70.

Grains per gallon to grammes per litre, divide by 70.

Degrees Fahr. to degrees Centigrade—Subtract 32, multiply the result by 5, and then divide by 9.

Degrees Centigrade to degrees Fahr.—Multiply by 9, divide by 5, and *add* 32.

Freezing Mixtures :—

Hydrochloric acid, ...	8 parts by weight.
Sodium Sulphate, ...	5 ,, ,,
or,	
Pounded ice, ...	2 ,, ,,
Common salt, ...	1 part by weight.

APPENDIX C.

SPECTROSCOPY.

Qualitative work—*e.g.*, the observation of the absorption bands of blood pigments,—may be very simply carried out by means of a small direct vision spectroscope.*

The usual form consists of inner and outer tubes—the outer having a vertical slit which can be widened or narrowed by a circular screw.

The inside tube has an arrangement of alternating crown-glass and flint prisms separated from the slit by a lens. At the other end, there is a round opening through which the observer looks. White light is broken up by the series of prisms, and this dispersion constitutes the spectrum.

Method of employment :—

1. Point the slit end of the instrument to the light (preferably at a white cloud), also taking care that the slit is not too widely opened.
2. Focus the eye-piece until the Fraunhofer lines in the spectrum are sharply defined.
3. Then place some of the urine to be examined in a test-tube and hold in front of the slit, taking care to focus the light passing through the test-tube as a sharp line on the slit.†

Refer to the plates for the various spectra, comparing the appearance observed with that of the ordinary spectrum.

For further information on the subject refer to any standard work on Physiology, where a full description of the various spectra will be found.

---

* Some of the varieties of such instruments may, for the reader's convenience, be stated, as well as their prices. Reynolds & Branson, of Leeds, supply an instrument of the kind for £1, 3s. Reichert's "Pocket Spectroscope" costs two guineas, and a more elaborate form, with a lateral scale for measurements, costs £3, 15s. Browning's (London), Miniature Spectroscope, with micrometer scale and comparison spectrum, costs £3, 10s. The last mentioned is a very convenient instrument.

† The test-tube acts as a cylindrical lens, and hence the light passing through it requires to be sharply focussed on the slit of the spectroscope.

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